

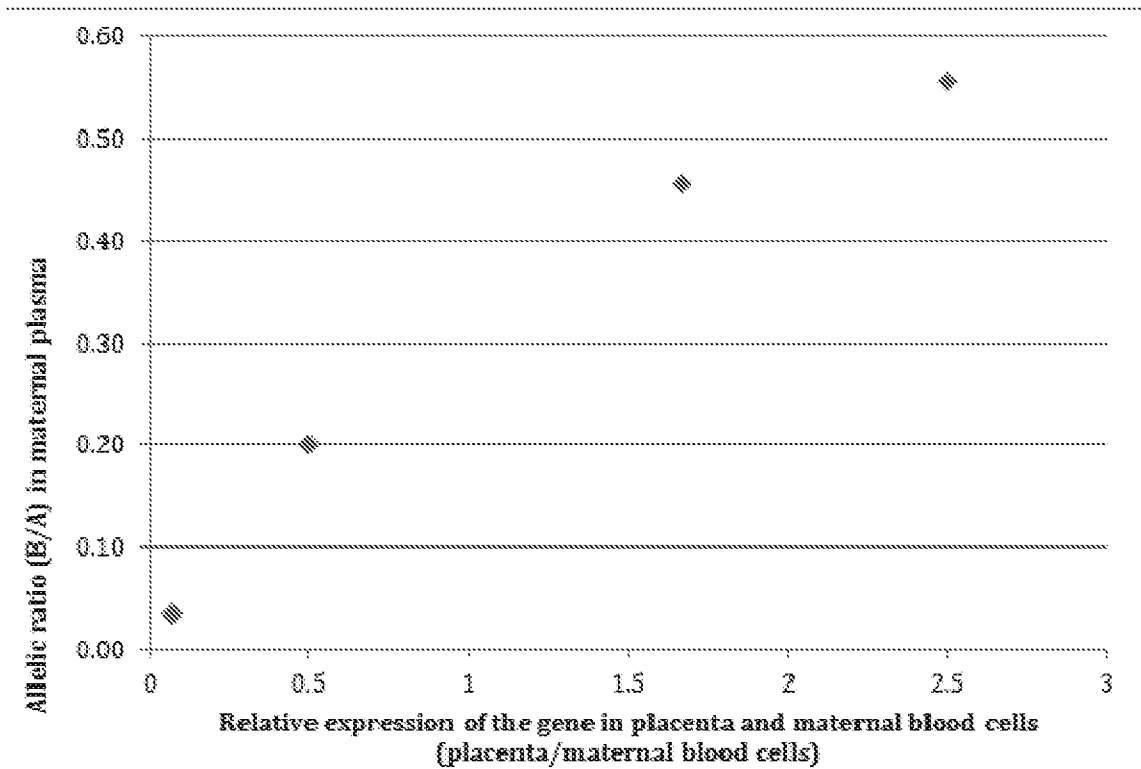


FIG. 1

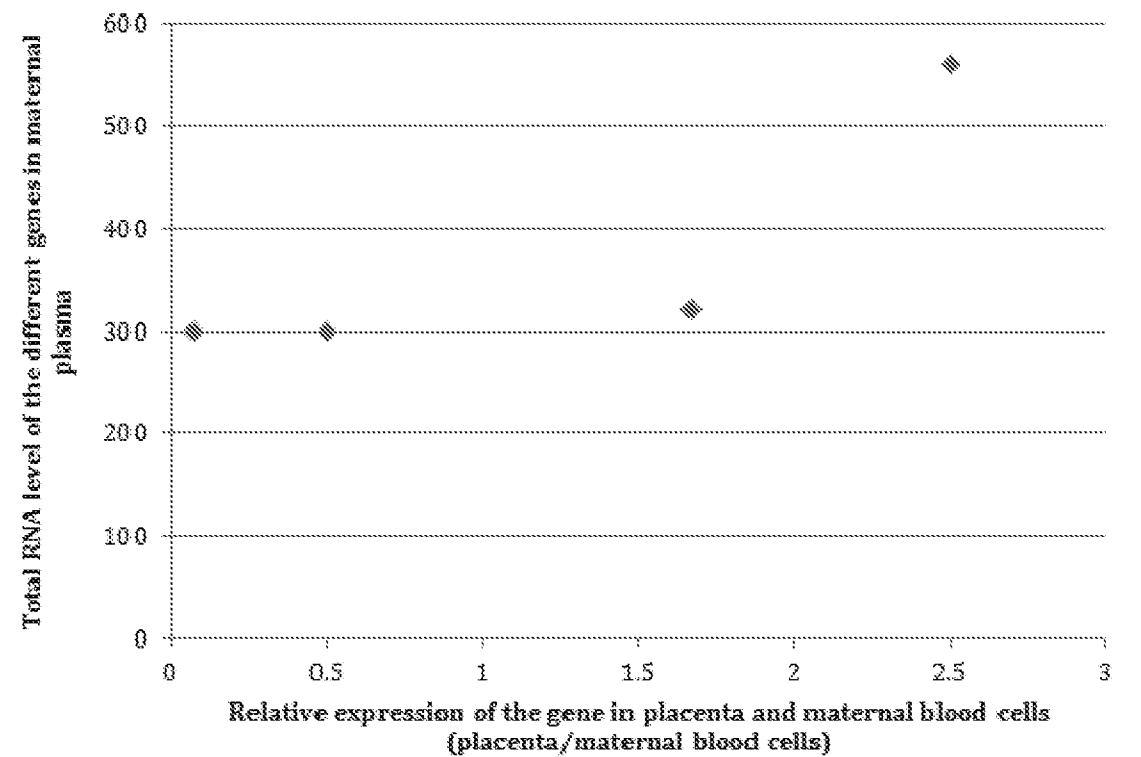


FIG. 2

2/29

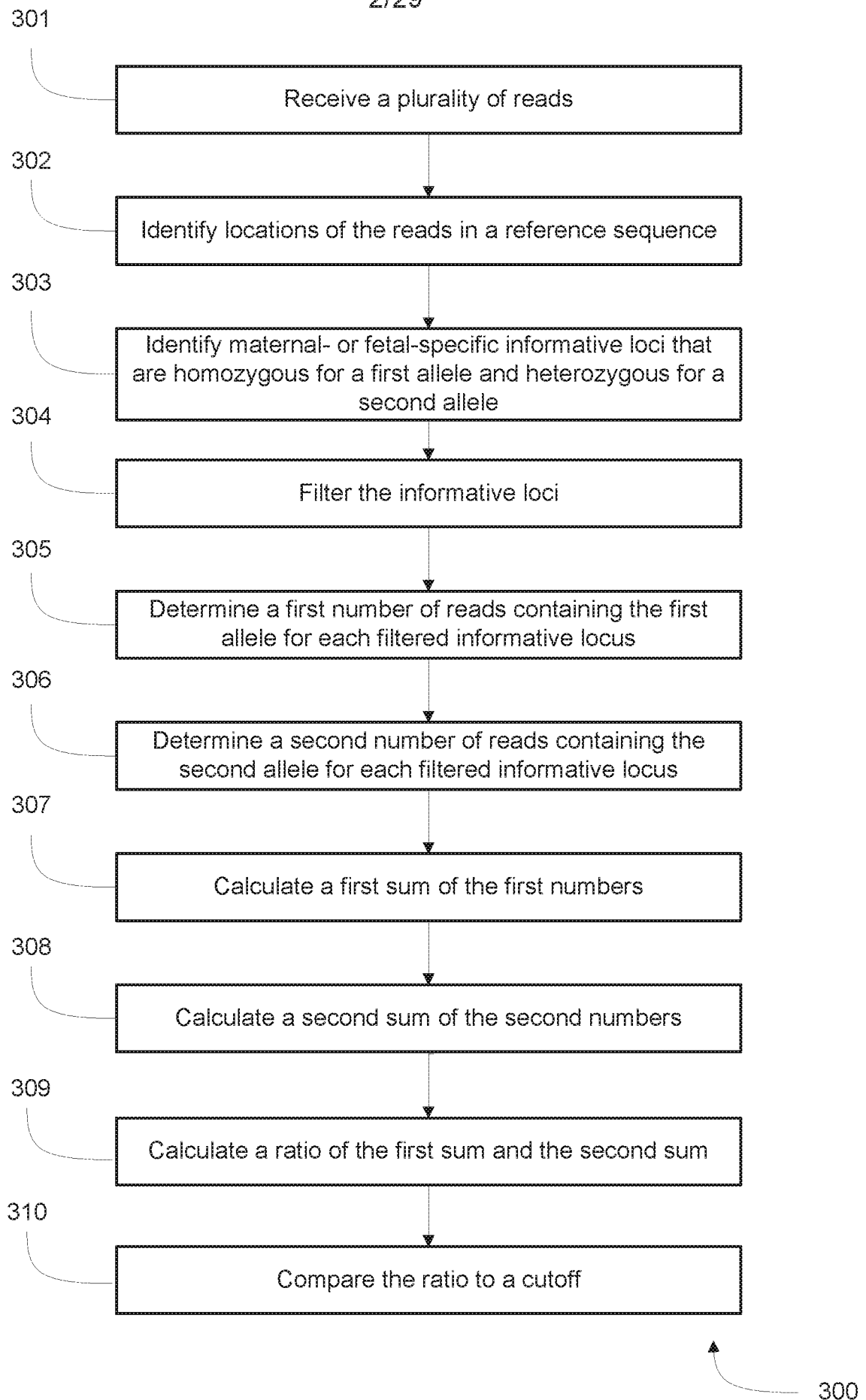


FIG. 3

3/29

| Sample type                      | Sample  | Raw reads   | Preprocessed <sup>a</sup><br>reads | (%) <sup>b</sup> | Mappable reads <sup>c</sup> | (%) <sup>d</sup> |
|----------------------------------|---------|-------------|------------------------------------|------------------|-----------------------------|------------------|
| Non-pregnant<br>female plasma    | CTR081  | 180,080,810 | 23,012,332                         | 12.78%           | 7,708,011                   | 33.50%           |
|                                  | CTR082  | 132,567,446 | 20,559,146                         | 15.51%           | 6,848,249                   | 33.31%           |
| Pre-delivery<br>maternal plasma  | M9600P  | 367,301,939 | 45,255,199                         | 12.32%           | 16,849,461                  | 37.23%           |
|                                  | M9549P  | 597,724,438 | 151,243,195                        | 25.30%           | 34,627,313                  | 22.90%           |
|                                  | M9356P  | 820,742,404 | 190,030,278                        | 23.15%           | 14,091,631                  | 7.42%            |
|                                  | M9415P  | 970,145,241 | 143,615,377                        | 14.80%           | 41,517,504                  | 28.91%           |
| Post-delivery<br>maternal plasma | M9356BP | 587,698,232 | 132,012,632                        | 22.46%           | 7,828,124                   | 5.93%            |
|                                  | M9415BP | 853,401,365 | 101,070,496                        | 11.84%           | 26,707,674                  | 26.42%           |
| Placenta                         | N9356   | 202,711,386 | 169,500,629                        | 83.62%           | 160,417,620                 | 94.64%           |
|                                  | N9415   | 257,219,381 | 203,094,642                        | 78.96%           | 193,126,555                 | 95.09%           |
| Maternal blood<br>cells          | M9600W  | 163,832,386 | 38,707,658                         | 23.63%           | 11,348,398                  | 29.32%           |
|                                  | M9549W  | 240,383,043 | 83,922,150                         | 34.91%           | 73,117,147                  | 87.12%           |
|                                  | M9356W  | 208,400,902 | 60,851,642                         | 29.20%           | 54,974,158                  | 90.34%           |
|                                  | M9415W  | 265,636,207 | 49,943,628                         | 18.80%           | 42,670,781                  | 85.44%           |

a. Retained reads after removal of highly repetitive reads.

b. % of the raw reads.

c. See Supplemental Data Table 2B for detailed breakdown.

d. % of the preprocessed reads.

**FIG. 4**

4/29

| Sample type                   | Sample  | Filtered reads <sup>a</sup> | Analyzable reads <sup>b</sup> | Exon (%) | Intron (%) | Intergenic region (%) <sup>c</sup> |
|-------------------------------|---------|-----------------------------|-------------------------------|----------|------------|------------------------------------|
| Non-pregnant female plasma    | CTR081  | 4,186,990                   | 3,521,021                     | 64.00%   | 6.47%      | 29.53%                             |
|                               | CTR082  | 3,594,966                   | 3,253,283                     | 61.93%   | 7.29%      | 30.78%                             |
| Pre-delivery maternal plasma  | M9600P  | 7,711,430                   | 9,138,031                     | 64.42%   | 6.47%      | 29.10%                             |
|                               | M9549P  | 20,481,388                  | 14,145,925                    | 41.84%   | 13.16%     | 45.00%                             |
|                               | M9356P  | 1,683,896                   | 12,407,735                    | 56.80%   | 30.76%     | 12.45%                             |
|                               | M9415P  | 23,164,778                  | 18,352,726                    | 53.61%   | 10.80%     | 35.59%                             |
| Post-delivery maternal plasma | M9356BP | 988,066                     | 6,840,058                     | 50.41%   | 38.15%     | 11.44%                             |
|                               | M9415BP | 15,853,377                  | 10,854,297                    | 50.12%   | 13.68%     | 36.19%                             |
| Placenta                      | N9356   | 3,204,907                   | 157,212,713                   | 31.18%   | 55.89%     | 12.93%                             |
|                               | N9415   | 4,186,711                   | 188,939,844                   | 26.51%   | 59.59%     | 13.90%                             |
| Maternal blood cells          | M9600W  | 854,869                     | 10,493,529                    | 69.71%   | 23.50%     | 6.79%                              |
|                               | M9549W  | 8,120,655                   | 64,996,492                    | 66.98%   | 26.67%     | 6.36%                              |
|                               | M9356W  | 4,255,081                   | 50,719,077                    | 69.13%   | 24.70%     | 6.16%                              |
|                               | M9415W  | 5,318,314                   | 37,352,467                    | 85.68%   | 10.74%     | 3.58%                              |

a. Filtered reads are mostly the nuclear and mitochondrial rRNAs and tRNAs.

b. Analyzable reads = total mappable reads – filtered reads.

c. % of reads that aligned to regions outside exons and introns of the reference genes.

FIG. 5

5/29

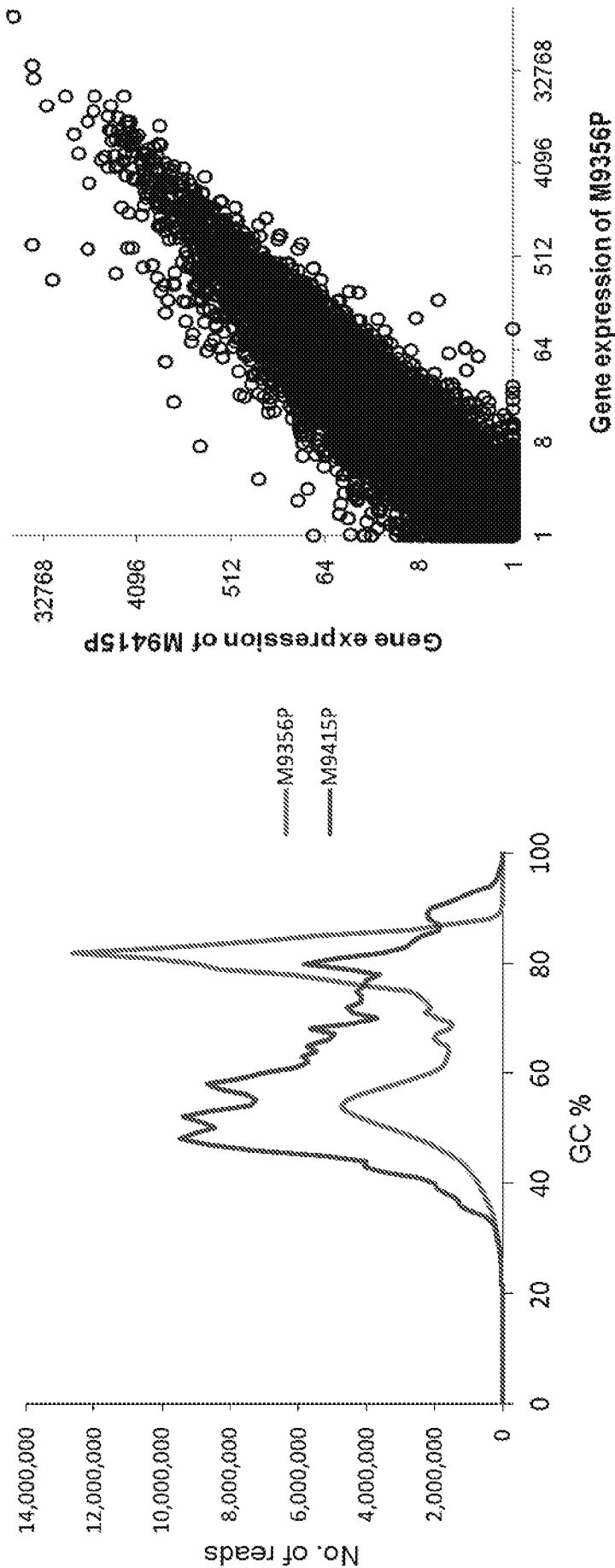


FIG. 6A

FIG. 6B

6/29

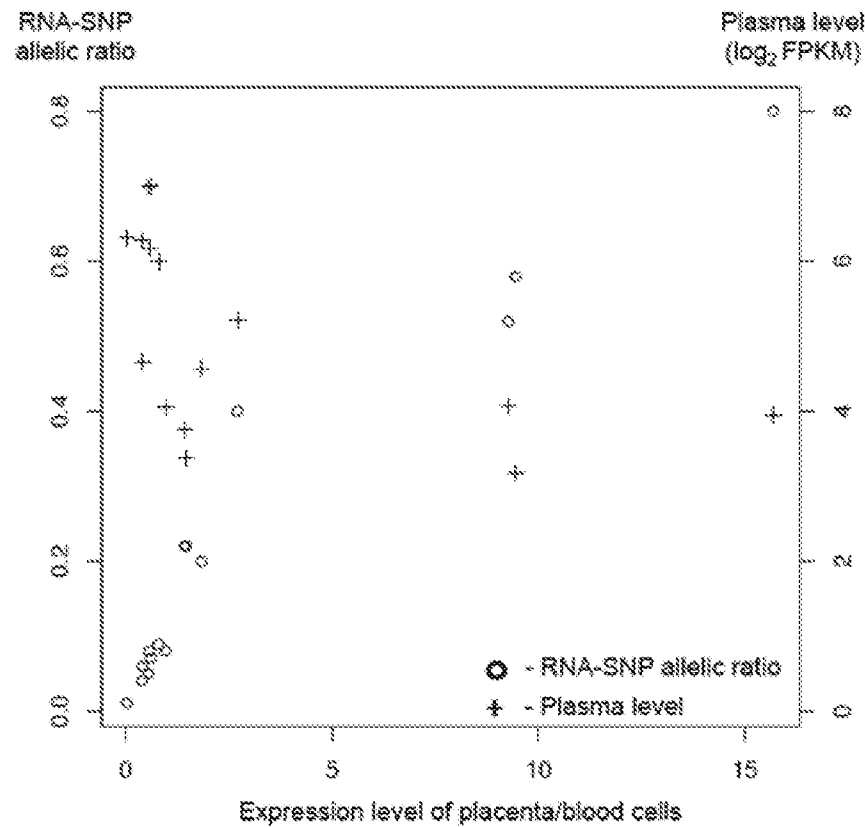


FIG. 7

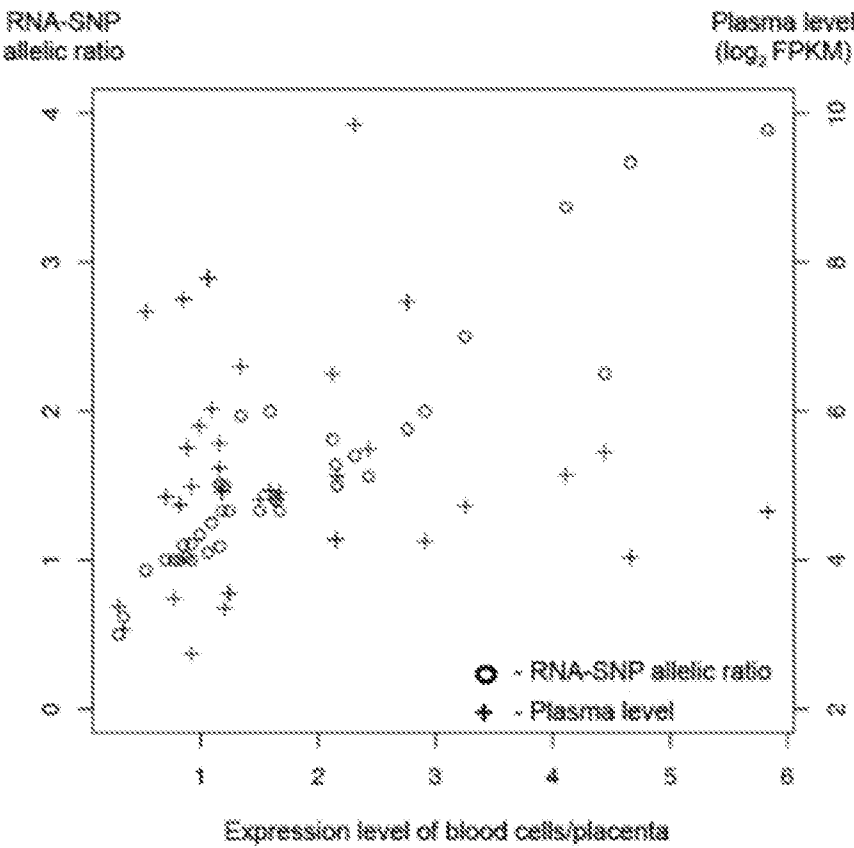


FIG. 8

7/29

| Fetal-specific SNP alleles (Maternal: AA, Fetal: AB) | SNPs              | Fetal allele/shared allele ratio | Average RNA-SNP ratio per gene | Placenta FPKM | Blood cell FPKM | Fold-difference (Placenta/Blood cell) | Plasma FPKM |
|------------------------------------------------------|-------------------|----------------------------------|--------------------------------|---------------|-----------------|---------------------------------------|-------------|
| AFF1                                                 | SNP 7:rs342462    | 0.28                             | 0.52                           | 149.731       | 16.1598         | 9.27                                  | 16.7037     |
|                                                      | SNP 8:rs342459    | 1                                |                                |               |                 |                                       |             |
|                                                      | SNP 9:rs10029915  | 0.29                             |                                |               |                 |                                       |             |
| SH3BGR2                                              | SNP 13:rs1507     | 0.07                             | 0.07                           | 24.7477       | 40.3078         | 0.61                                  | 128.2908    |
| SLC38A1                                              | SNP 3:rs3742058   | 0.17                             | 0.58                           | 142.8723      | 15.1123         | 9.45                                  | 9.0209      |
|                                                      | SNP 4:rs3742059   | 1                                |                                |               |                 |                                       |             |
| PTTG1P                                               | SNP 6:rs873317    | 0.4                              | 0.4                            | 152.8104      | 56.4153         | 2.71                                  | 37.1191     |
| GMAP1-GMAP5                                          | SNP 14:rs1046355  | 0.04                             | 0.04                           | 15.9771       | 39.9271         | 0.4                                   | 77.4282     |
| CTSS                                                 | SNP 1:rs3754212   | 0.01                             | 0.01                           | 11.0084       | 382.8589        | 0.03                                  | 79.3012     |
| RHOBTB3                                              | SNP 10:rs34896    | 1                                | 0.8                            | 338.5763      | 21.5841         | 15.69                                 | 15.4046     |
|                                                      | SNP 11:rs34898    | 0.6                              |                                |               |                 |                                       |             |
|                                                      | SNP 12:rs34899    | 0.8                              |                                |               |                 |                                       |             |
| ARHGEF12                                             | SNP 2:rs192719576 | 0.09                             | 0.09                           | 88.5256       | 110.1833        | 0.8                                   | 63.7037     |
| TXNRP1                                               | SNP 5:rs1111979   | 0.2                              | 0.2                            | 65.9309       | 35.795          | 1.84                                  | 23.6787     |
| HPCAL1                                               | SNP 11:rs2270302  | 0.06                             | 0.06                           | 17.2498       | 42.5469         | 0.41                                  | 25.2768     |
| RAB4A                                                | SNP 2:rs15452     | 0.08                             | 0.08                           | 12.7741       | 22.2066         | 0.58                                  | 72.2382     |
| PGM2                                                 | SNP 13:rs3752683  | 0.22                             | 0.22                           | 33.0576       | 23.045          | 1.43                                  | 13.4293     |
| PSMB3                                                | SNP 10:rs228274   | 0.05                             | 0.05                           | 65.0683       | 117.5188        | 0.55                                  | 127.3262    |
| ADIPOR2                                              | SNP 4:rs12342     | 0.08                             | 0.08                           | 18.1942       | 18.7699         | 0.97                                  | 16.5717     |
|                                                      | SNP 5:rs1044471   | 0.08                             |                                |               |                 |                                       |             |
| CHFR                                                 | SNP 9:rs35011845  | 0.22                             | 0.22                           | 21.9501       | 15.0583         | 1.46                                  | 10.3748     |

FIG. 9

8/29

| Maternal-specific SNP alleles (Maternal: AB, Fetal: AA) | SNPs               | Maternal allele/shared allele ratio | Average RNA-SNP ratio per gene | Placenta FPKM | Blood cell FPKM | Fold-difference (Blood cell/Placenta) | Plasma FPKM |
|---------------------------------------------------------|--------------------|-------------------------------------|--------------------------------|---------------|-----------------|---------------------------------------|-------------|
| AKAP10                                                  | SNP 18:rs2108978   | 1.33                                | 1.33                           | 22.414        | 18.1324         | 1.24                                  | 11.7168     |
| EIF2S2                                                  | SNP 37:rs4911406   | 1.25                                | 1.25                           | 39.3008       | 35.9748         | 1.09                                  | 65.1988     |
| IHDM1D                                                  | SNP 51:rs76676651  | 1.4                                 | 1.4                            | 43.0656       | 26.1836         | 1.64                                  | 28.1734     |
| USP47                                                   | SNP 5:rs11022079   | 0.5                                 | 0.5                            | 10.735        | 36.1867         | 0.3                                   | 10.3945     |
| PPP4R2                                                  | SNP 6:rs148238084  | 0.5                                 |                                |               |                 |                                       |             |
|                                                         | SNP 40:rs61188513  | 1.09                                | 1.09                           | 80.3628       | 69.563          | 1.16                                  | 47.4149     |
|                                                         | SNP 15:rs4779520   | 0.78                                | 1.64                           | 22.9283       | 10.6869         | 2.15                                  | 19.3486     |
| KLF13                                                   | SNP 16:rs6493629   | 2.5                                 |                                |               |                 |                                       |             |
| FAM107B                                                 | SNP 4:rs11259151   | 2                                   | 2                              | 24.1097       | 15.1776         | 1.59                                  | 30.5864     |
| APOL2                                                   | SNP 39:rs132759    | 1.33                                | 1.33                           | 17.9996       | 12.0226         | 1.5                                   | 28.1601     |
|                                                         | SNP 10:rs2389910   | 1.56                                | 1.11                           | 27.2282       | 29.7396         | 0.92                                  | 31.7672     |
| RAP2A                                                   | SNP 11:rs12873919  | 0.67                                |                                |               |                 |                                       |             |
|                                                         | SNP 1:rs117963129  | 4                                   | 3.37                           | 48.3896       | 11.7589         | 4.11                                  | 35.3443     |
|                                                         | SNP 2:rs1055184    | 5                                   |                                |               |                 |                                       |             |
| RIT1                                                    | SNP 3:rs493446     | 1.12                                |                                |               |                 |                                       |             |
| STK17A                                                  | SNP 48:rs56286238  | 1.33                                | 1.33                           | 61.0052       | 36.447          | 1.67                                  | 30.0074     |
|                                                         | SNP 23:rs14031     | 0.5                                 | 0.62                           | 11.0432       | 32.3155         | 0.34                                  | 8.3988      |
| C19orf63                                                | SNP 24:rs1046246   | 0.75                                |                                |               |                 |                                       |             |
| SMK1                                                    | SNP 14:rs10135595  | 1                                   | 1                              | 27.1212       | 33.0441         | 0.82                                  | 26.8366     |
|                                                         | SNP 42:rs3797341   | 1.5                                 | 1.02                           | 26.837        | 30.3427         | 0.88                                  | 45.4491     |
|                                                         | SNP 43:rs3203922   | 0.78                                |                                |               |                 |                                       |             |
| TNFAIP8                                                 | SNP 44:rs1045242   | 0.79                                |                                |               |                 |                                       |             |
| CPEB4                                                   | SNP 46:rs12659398  | 1                                   | 1                              | 28.4523       | 40.5723         | 0.7                                   | 28.802      |
| PTPRJ                                                   | SNP 7:rs117902837  | 2                                   | 2                              | 59.7568       | 20.5437         | 2.91                                  | 19.0642     |
| RPL36                                                   | SNP 22:rs3810220   | 1.7                                 | 1.7                            | 152.2501      | 65.9528         | 2.31                                  | 921.8925    |
|                                                         | SNP 25:rs1137288   | 1.62                                | 1.88                           | 114.7107      | 41.6213         | 2.76                                  | 176.8333    |
|                                                         | SNP 26:rs3087895   | 2.17                                |                                |               |                 |                                       |             |
|                                                         | SNP 27:rs3768670   | 1.86                                |                                |               |                 |                                       |             |
| YPEL5                                                   | SNP 28:rs3768671   | 1.86                                |                                |               |                 |                                       |             |
|                                                         | SNP 53:rs114261839 | 1                                   | 1.33                           | 51.7974       | 43.9599         | 1.18                                  | 30.1847     |
|                                                         | SNP 54:rs208753    | 1.4                                 |                                |               |                 |                                       |             |
|                                                         | SNP 55:rs17635381  | 2.27                                |                                |               |                 |                                       |             |
| PCM1                                                    | SNP 56:rs6991775   | 0.67                                |                                |               |                 |                                       |             |
| UBR2                                                    | SNP 47:rs6916713   | 2.25                                | 2.25                           | 102.9892      | 23.2007         | 4.44                                  | 43.5569     |
|                                                         | SNP 32:rs3747      | 1.22                                | 1.97                           | 50.467        | 37.5349         | 1.34                                  | 96.8859     |
|                                                         | SNP 33:rs9579      | 2.17                                |                                |               |                 |                                       |             |
|                                                         | SNP 34:rs3088214   | 2.89                                |                                |               |                 |                                       |             |
| TNS1                                                    | SNP 35:rs1063281   | 1.62                                |                                |               |                 |                                       |             |
| EIF4A1                                                  | SNP 17:rs1057086   | 0.93                                | 0.93                           | 70.1974       | 132.2932        | 0.53                                  | 161.6599    |
| BACH1                                                   | SNP 38:rs15092     | 2.5                                 | 2.5                            | 112.4409      | 34.6219         | 3.25                                  | 26.4284     |
|                                                         | SNP 49:rs6850      | 1.11                                | 1.05                           | 66.7742       | 62.9202         | 1.06                                  | 220.7639    |
| PPIA                                                    | SNP 50:rs6904      | 1                                   |                                |               |                 |                                       |             |
| TMX1                                                    | SNP 12:rs7160810   | 1                                   | 1                              | 11.8758       | 12.8978         | 0.92                                  | 6.7127      |
| ANKRD44                                                 | SNP 29:rs3731569   | 3.67                                | 3.67                           | 65.5013       | 14.0504         | 4.66                                  | 16.412      |
|                                                         | SNP 57:rs3398      | 0.33                                | 1.51                           | 43.1289       | 37.048          | 1.16                                  | 37.6685     |
| ZFAND5                                                  | SNP 58:rs969       | 2.69                                |                                |               |                 |                                       |             |
|                                                         | SNP 19:rs12327477  | 0.67                                | 3.89                           | 171.6269      | 29.4281         | 5.83                                  | 25.153      |
|                                                         | SNP 20:rs2304859   | 7                                   |                                |               |                 |                                       |             |
| SMCHD1                                                  | SNP 21:rs7238459   | 4                                   |                                |               |                 |                                       |             |
| NR3C1                                                   | SNP 45:rs6191      | 1                                   | 1                              | 28.0561       | 36.5516         | 0.77                                  | 11.2138     |
| CRNKL1                                                  | SNP 36:rs2255255   | 1.5                                 | 1.5                            | 15.8244       | 13.148          | 1.2                                   | 10.1897     |
| CALM1                                                   | SNP 13:rs5871      | 1.1                                 | 1.1                            | 76.0647       | 89.0949         | 0.85                                  | 181.3474    |
| FDFT1                                                   | SNP 52:rs79708434  | 1.56                                | 1.56                           | 83.9629       | 34.6215         | 2.43                                  | 44.9826     |
|                                                         | SNP 30:rs1051677   | 1                                   | 1.17                           | 74.6452       | 75.2029         | 0.99                                  | 55.8144     |
| XRCC5                                                   | SNP 31:rs2440      | 1.33                                |                                |               |                 |                                       |             |
|                                                         | SNP 8:rs3741380    | 2.75                                | 1.81                           | 29.7293       | 14.0146         | 2.12                                  | 90.3776     |
| EHBPI11                                                 | SNP 9:rs6591182    | 0.88                                |                                |               |                 |                                       |             |
| OPA1                                                    | SNP 41:rs7643844   | 1.5                                 | 1.5                            | 49.1647       | 22.7367         | 2.16                                  | 34.8335     |

FIG. 10

9/29

RNA-SNP  
allelic ratio

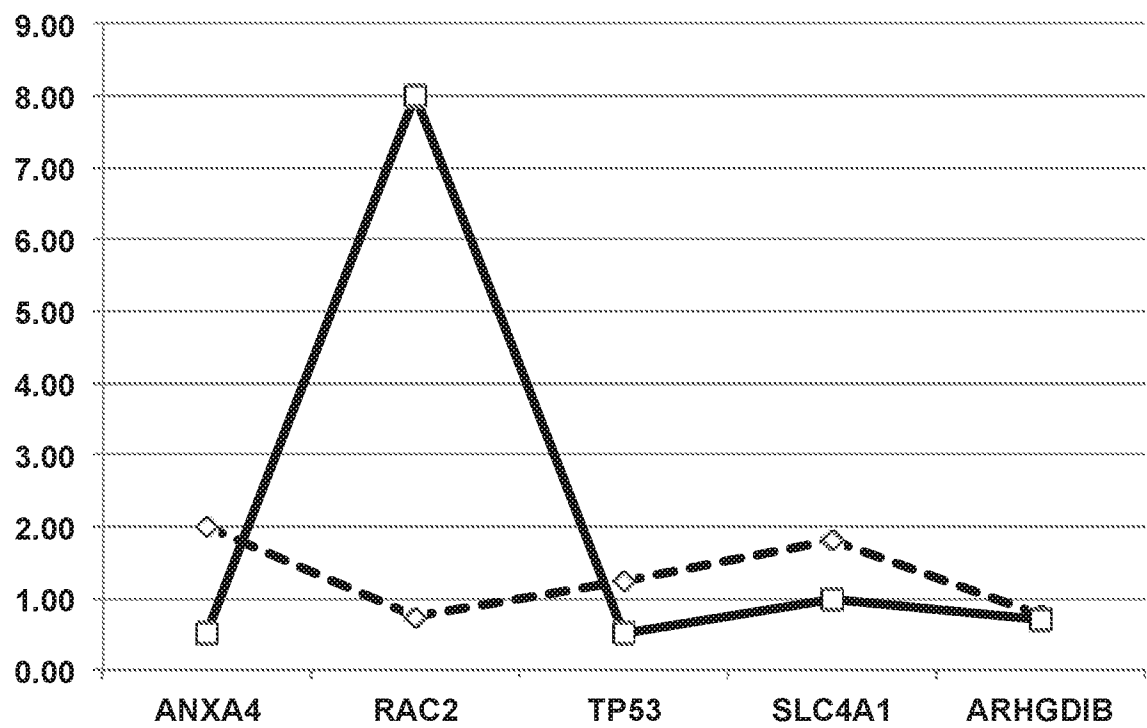


FIG. 11A

Fold-  
differences

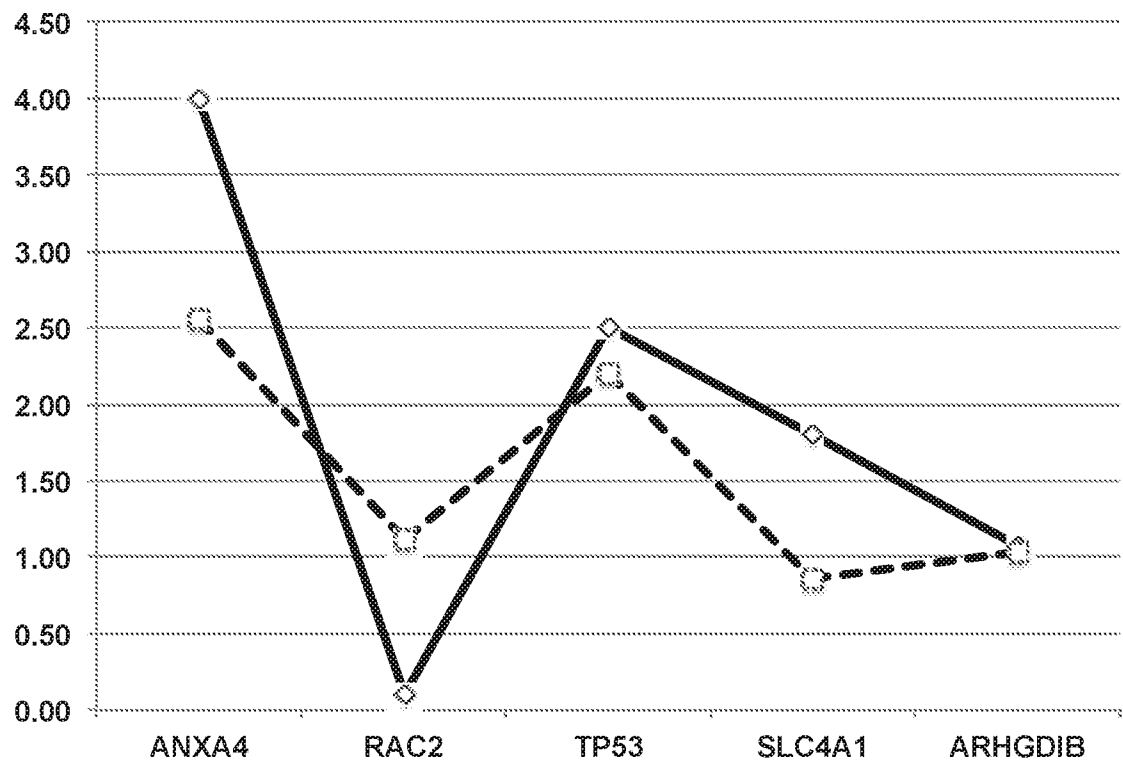


FIG. 11B

10/29

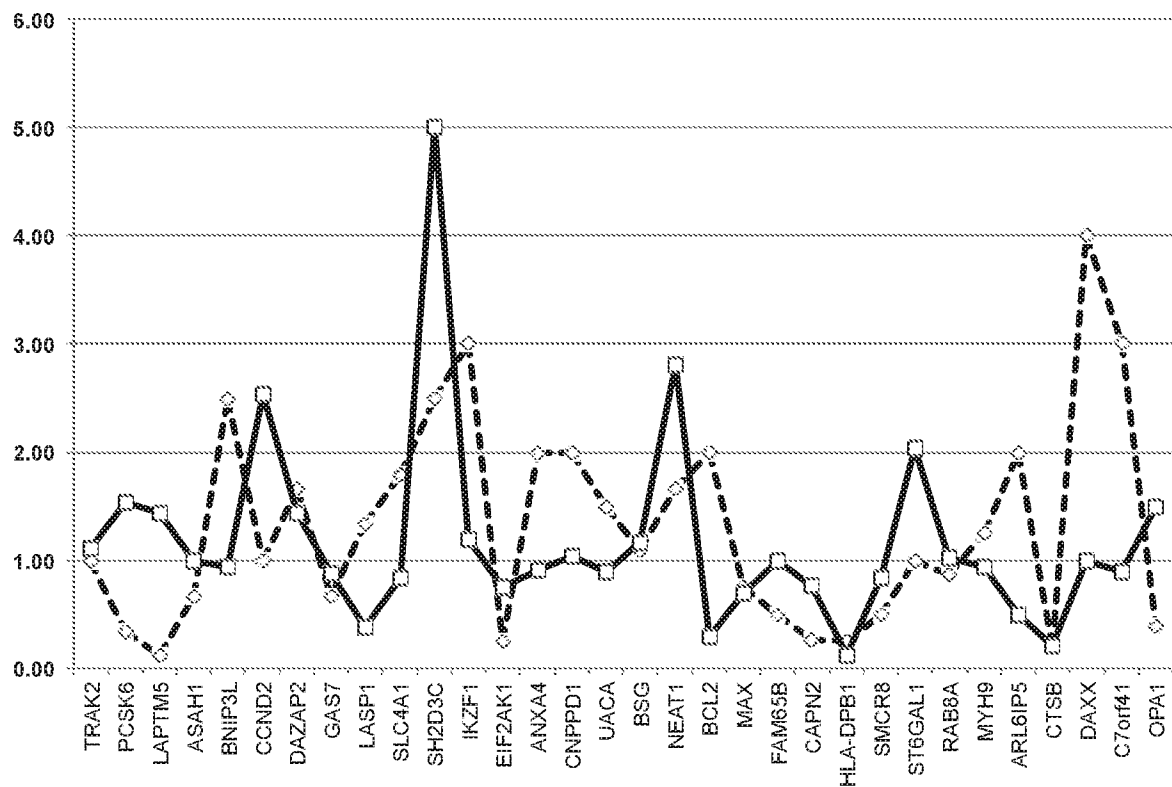
RNA-SNP  
allelic ratio

FIG. 12A

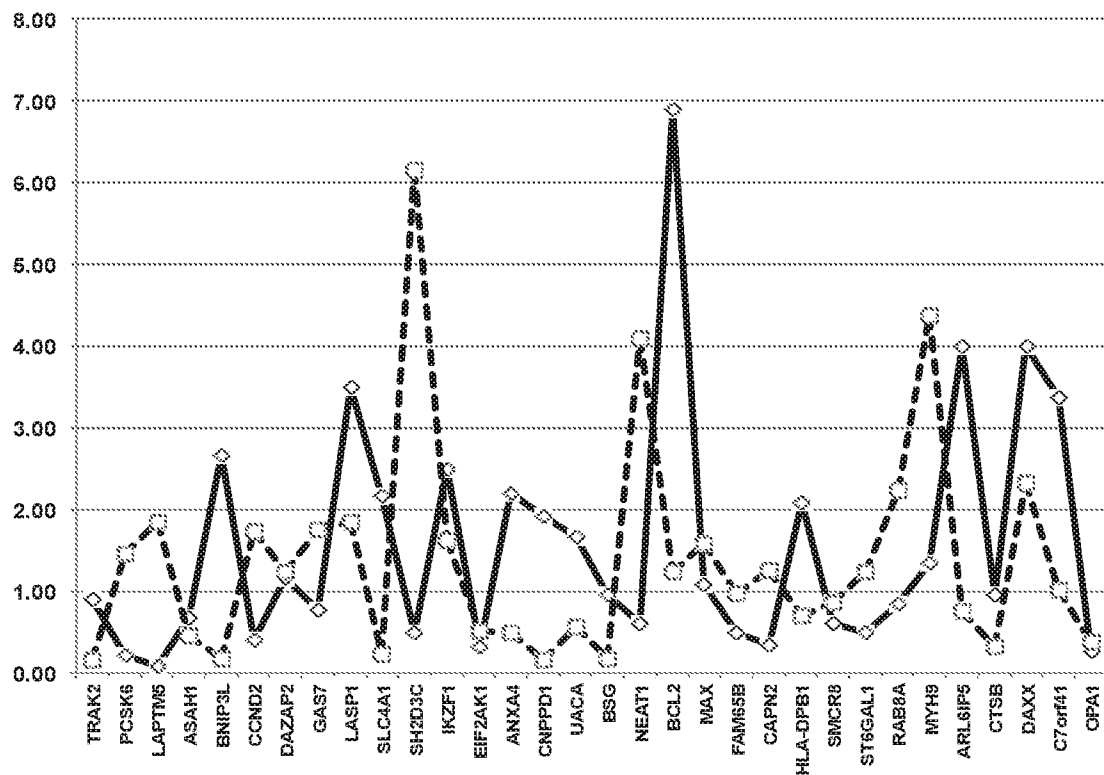
Fold-  
differences

FIG. 12B

11/29

| Maternal-specific SNP alleles (Maternal: AB, Fetal: AA) | 5641 (PET) (GA: 36 6/7) |                                     |                                | 7171 (Normal) (GA: 36 6/7) |                                     |                                | Fold-changes of RNA-SNP ratio for each gene (5641 vs 7171) |  | Expression level in the plasma |           | Fold-changes of FPKM (5641 vs 7171) |
|---------------------------------------------------------|-------------------------|-------------------------------------|--------------------------------|----------------------------|-------------------------------------|--------------------------------|------------------------------------------------------------|--|--------------------------------|-----------|-------------------------------------|
|                                                         | SNPs                    | Maternal allele/shared allele ratio | Average RNA-SNP ratio per gene | SNPs                       | Maternal allele/shared allele ratio | Average RNA-SNP ratio per gene |                                                            |  | 5641 FPKM                      | 7171 FPKM |                                     |
| ANXA4                                                   | SNP 1: kgp9682337       | 2                                   | 2                              | SNP 9: rs6546548           | 0.5                                 | 0.5                            | 4                                                          |  | 12.1379                        | 4.7565    | 2.551855356                         |
| RAC2                                                    | SNP 3: rs6672           | 0.75                                | 0.75                           | SNP 8: rs2239774           | 8                                   | 8                              | 0.09375                                                    |  | 319.973                        | 268.0231  | 1.110928255                         |
| TP53                                                    | SNP 2: rs17879353       | 0.5                                 | 1.25                           | SNP 4: rs1042522           | 0.5                                 | 0.5                            | 2.5                                                        |  | 28.9503                        | 13.1548   | 2.200740414                         |
| SLC4A1                                                  | SNP 4: rs1042522        | 2                                   |                                |                            |                                     |                                |                                                            |  |                                |           |                                     |
| ARHGD1B                                                 | SNP 5: rs5035           | 1.8                                 | 1.8                            | SNP 7: rs2072081           | 1                                   | 1                              | 1.8                                                        |  | 165.1352                       | 192.3307  | 0.8588600317                        |
|                                                         | SNP 6: kgp668929        | 0.76                                | 0.76                           | SNP 6: kgp668929           | 0.71                                | 0.71                           | 1.070422535                                                |  | 665.6615                       | 640.9633  | 1.038532939                         |

FIG. 13

12/29

| Maternal-specific SNP alleles (Maternal: AB, Fetal: AA) | 5641 (PET) (GA: 36 6/7)                                                       |                                     |                                | 9356 (Normal) (GA: 37 2/7)                                                                       |                                      |                                | Fold-changes of RNA-SNP ratio for each gene (5641 vs 7171) | Expression level in the plasma |           |                                     |
|---------------------------------------------------------|-------------------------------------------------------------------------------|-------------------------------------|--------------------------------|--------------------------------------------------------------------------------------------------|--------------------------------------|--------------------------------|------------------------------------------------------------|--------------------------------|-----------|-------------------------------------|
|                                                         | SNPs                                                                          | Maternal allele/shared allele ratio | Average RNA-SNP ratio per gene | SNPs                                                                                             | Maternal allele/shared allele ratio  | Average RNA-SNP ratio per gene |                                                            | 5641 FPKM                      | 9356 FPKM | Fold-changes of FPKM (5641 vs 7171) |
| TRAK2                                                   | SNP 2.kgp14544935                                                             | 1                                   | 1                              | SNP 62.rs11898629<br>SNP 63.rs3795966<br>SNP 64.rs13022344                                       | 0.8<br>1.47<br>1.04                  | 1.11                           | 0.90909091                                                 | 95.0691                        | 818.1783  | 0.153729125                         |
| IPC5K8                                                  | SNP 26.kgp8258505                                                             | 0.33                                | 0.33                           | SNP 48.rs1058280                                                                                 | 1.54                                 | 1.54                           | 0.214285714                                                | 22.3438                        | 15.3949   | 1.451376755                         |
| LAPTM5                                                  | SNP 7.kgp15703060                                                             | 0.12                                | 0.12                           | SNP 38.rs8048                                                                                    | 1.43                                 | 1.43                           | 0.083916084                                                | 215.8869                       | 117.3578  | 1.83956158                          |
| ASAH1                                                   | SNP 3.kgp3689333                                                              | 0.67                                | 0.67                           | SNP 85.rs71528182                                                                                | 1                                    | 1                              | 0.67                                                       | 35.6956                        | 78.8371   | 0.452776675                         |
| BNIP3L                                                  | SNP 5.rs17310286                                                              | 2.5                                 | 2.5                            | SNP 5.rs17310286<br>SNP 86.rs1042592                                                             | 1.09<br>0.78                         | 0.94                           | 2.659574468                                                | 139.6533                       | 783.6419  | 0.178210609                         |
| CCND2                                                   | SNP 11.rs1049606                                                              | 1                                   | 1                              | SNP 11.rs1049606<br>SNP 42.rs3217925                                                             | 1.07<br>4                            | 2.54                           | 0.393700787                                                | 39.864                         | 22.9748   | 1.735116478                         |
| DAZAP2                                                  | SNP 25.kgp1918624                                                             | 1.67                                | 1.67                           | SNP 43.rs1049487                                                                                 | 1.43                                 | 1.43                           | 1.167832168                                                | 104.3778                       | 84.1193   | 1.240830582                         |
| GAS7                                                    | SNP 31.rs2240739                                                              | 0.67                                | 0.67                           | SNP 49.rs14383<br>SNP 50.rs16958968                                                              | 0.25<br>1.5                          | 0.89                           | 0.761363636                                                | 12.6931                        | 7.2272    | 1.756295661                         |
| LASP1                                                   | SNP 29.kgp8906974                                                             | 1.33                                | 1.33                           | SNP 53.rs11538845                                                                                | 0.38                                 | 0.38                           | 3.5                                                        | 72.978                         | 39.5819   | 1.843670971                         |
| SLC4A1                                                  | SNP 4.rs5035                                                                  | 1.8                                 | 1.8                            | SNP 54.rs13308788                                                                                | 0.83                                 | 0.83                           | 2.168674699                                                | 165.1352                       | 726.2616  | 0.227377022                         |
| SH2D3C                                                  | SNP 17.rs514024                                                               | 2.5                                 | 2.5                            | SNP 87.rs35019975                                                                                | 5                                    | 5                              | 0.5                                                        | 31.7735                        | 5.1573    | 6.160872754                         |
| IKZF1                                                   | SNP 21.kgp5028738                                                             | 3                                   | 3                              | SNP 82.rs72645704<br>SNP 83.rs72645705                                                           | 1.6<br>0.8                           | 1.2                            | 2.5                                                        | 45.9371                        | 28.2684   | 1.625933606                         |
| EF2AK1                                                  | SNP 22.rs2639                                                                 | 0.25                                | 0.25                           | SNP 79.rs2640<br>SNP 22.rs2639                                                                   | 0.8<br>0.71                          | 0.75                           | 0.333333333                                                | 89.0985                        | 133.6252  | 0.517106803                         |
| ANKA4                                                   | SNP 1.kgp9682337                                                              | 2                                   | 2                              | SNP 61.rs2226203                                                                                 | 0.91                                 | 0.91                           | 2.197802198                                                | 12.1379                        | 24.8486   | 0.4884742                           |
| CNPPD1                                                  | SNP 8.rs1043160                                                               | 2                                   | 2                              | SNP 65.rs11236<br>SNP 86.rs1127102<br>SNP 8.rs1043160<br>SNP 87.rs1127101                        | 1.1<br>1.08<br>1.38<br>0.61          | 1.04                           | 1.923076923                                                | 26.7431                        | 163.7143  | 0.163352255                         |
| UACA                                                    | SNP 16.rs934005                                                               | 1.5                                 | 1.5                            | SNP 16.rs934005<br>SNP 47.rs4776525<br>SNP 47.rs4776525                                          | 1.6<br>0.2<br>0.2                    | 0.9                            | 1.666666667                                                | 12.9841                        | 23.1721   | 0.560333332                         |
| BSG                                                     | SNP 10.rs2229684                                                              | 1.1                                 | 1.1                            | SNP 56.rs4682<br>SNP 57.rs8637<br>SNP 58.rs8259                                                  | 1.2<br>1.32<br>0.96                  | 1.16                           | 0.948275862                                                | 151.0873                       | 867.8994  | 0.174084468                         |
| NEAT1                                                   | SNP 32.rs680413                                                               | 1.67                                | 1.67                           | SNP 32.rs680413<br>SNP 41.rs2238895                                                              | 1.12<br>4.5                          | 2.81                           | 0.59430605                                                 | 83.9749                        | 20.5134   | 4.093660729                         |
| BCL2                                                    | SNP 36.rs1564483                                                              | 2                                   | 2                              | SNP 55.rs4987857                                                                                 | 0.29                                 | 0.29                           | 6.896551724                                                | 13.6149                        | 11.001    | 1.237605672                         |
| MAX                                                     | SNP 16.rs4902359                                                              | 0.75                                | 0.75                           | SNP 44.rs4902357<br>SNP 45.rs1957949<br>SNP 46.rs1957948<br>SNP 18.rs4902359                     | 0.62<br>0.75<br>0.74<br>0.64         | 0.69                           | 1.086956522                                                | 186.4324                       | 117.3962  | 1.588061624                         |
| FAM65B                                                  | SNP 12.rs12183109                                                             | 0.5                                 | 0.5                            | SNP 77.rs11285                                                                                   | 1                                    | 1                              | 0.5                                                        | 38.9914                        | 39.9277   | 0.969036534                         |
| CAPN2                                                   | SNP 6.rs17568<br>SNP 13.kgp4535923                                            | 0.33<br>0.2                         | 0.27                           | SNP 39.rs3738383<br>SNP 6.rs17568<br>SNP 40.rs10961                                              | 0.92<br>0.48<br>0.93                 | 0.77                           | 0.350649351                                                | 59.5279                        | 47.4986   | 1.253255885                         |
| HLA-DPB1                                                | SNP 27.kgp4559778                                                             | 0.25                                | 0.25                           | SNP 78.rs41558014                                                                                | 0.12                                 | 0.12                           | 2.083333333                                                | 62.8314                        | 90.6768   | 0.692915939                         |
| SMCR8                                                   | SNP 35.rs3829856                                                              | 0.5                                 | 0.5                            | SNP 51.rs1563632<br>SNP 52.rs921985                                                              | 1<br>0.67                            | 0.83                           | 0.602409639                                                | 4.3801                         | 5.1181    | 0.855805665                         |
| ST8GAL1                                                 | SNP 19.rs2264749                                                              | 1                                   | 1                              | SNP 19.rs2264749<br>SNP 73.rs4686848<br>SNP 74.rs1801380<br>SNP 75.rs7559                        | 1.27<br>2<br>4.5<br>0.4              | 2.04                           | 0.490196078                                                | 15.0179                        | 12.2028   | 1.230692956                         |
| RAB6A                                                   | SNP 9.rs3745314<br>SNP 20.rs17722795<br>SNP 30.rs10408964<br>SNP 37.rs1043346 | 0.71<br>1.33<br>0.44<br>1           | 0.87                           | SNP 59.rs3745313<br>SNP 9.rs3745314<br>SNP 20.rs17722795<br>SNP 37.rs1043346<br>SNP 60.rs1043407 | 1.86<br>0.92<br>1.17<br>0.38<br>0.78 | 1.02                           | 0.852941176                                                | 150.8067                       | 67.5592   | 2.232216598                         |
| MYH9                                                    | SNP 28.kgp7015684                                                             | 1.25                                | 1.25                           | SNP 68.rs2481<br>SNP 69.rs7078<br>SNP 70.rs12107<br>SNP 71.rs11089787                            | 1.39<br>0.46<br>0.47<br>1.38         | 0.93                           | 1.344026022                                                | 547.5822                       | 125.4471  | 4.365044708                         |
| ARL6IP5                                                 | SNP 33.rs7038                                                                 | 2                                   | 2                              | SNP 72.rs60050966                                                                                | 0.5                                  | 0.5                            | 4                                                          | 57.8308                        | 77.8228   | 0.743104848                         |
| CTSB                                                    | SNP 34.kgp8442325                                                             | 0.2                                 | 0.2                            | SNP 64.rs138489256                                                                               | 0.21                                 | 0.21                           | 0.952300982                                                | 40.7539                        | 124.8545  | 0.326411143                         |
| DAXX                                                    | SNP 23.rs1059231                                                              | 4                                   | 4                              | SNP 23.rs1059231                                                                                 | 1                                    | 1                              | 4                                                          | 33.1412                        | 14.2532   | 2.325178101                         |
| C7orf41                                                 | SNP 15.rs2110394                                                              | 3                                   | 3                              | SNP 80.rs702829<br>SNP 81.rs3750089                                                              | 0.67<br>1.11                         | 0.89                           | 3.370786517                                                | 87.1367                        | 86.8271   | 1.003565707                         |
| OPA1                                                    | SNP 14.kgp7301324<br>SNP 24.kgp8804496                                        | 0.4<br>0.4                          | 0.4                            | SNP 76.rs7643844                                                                                 | 1.5                                  | 1.5                            | 0.266666667                                                | 13.0804                        | 34.8335   | 0.379512079                         |

FIG. 14

13/29

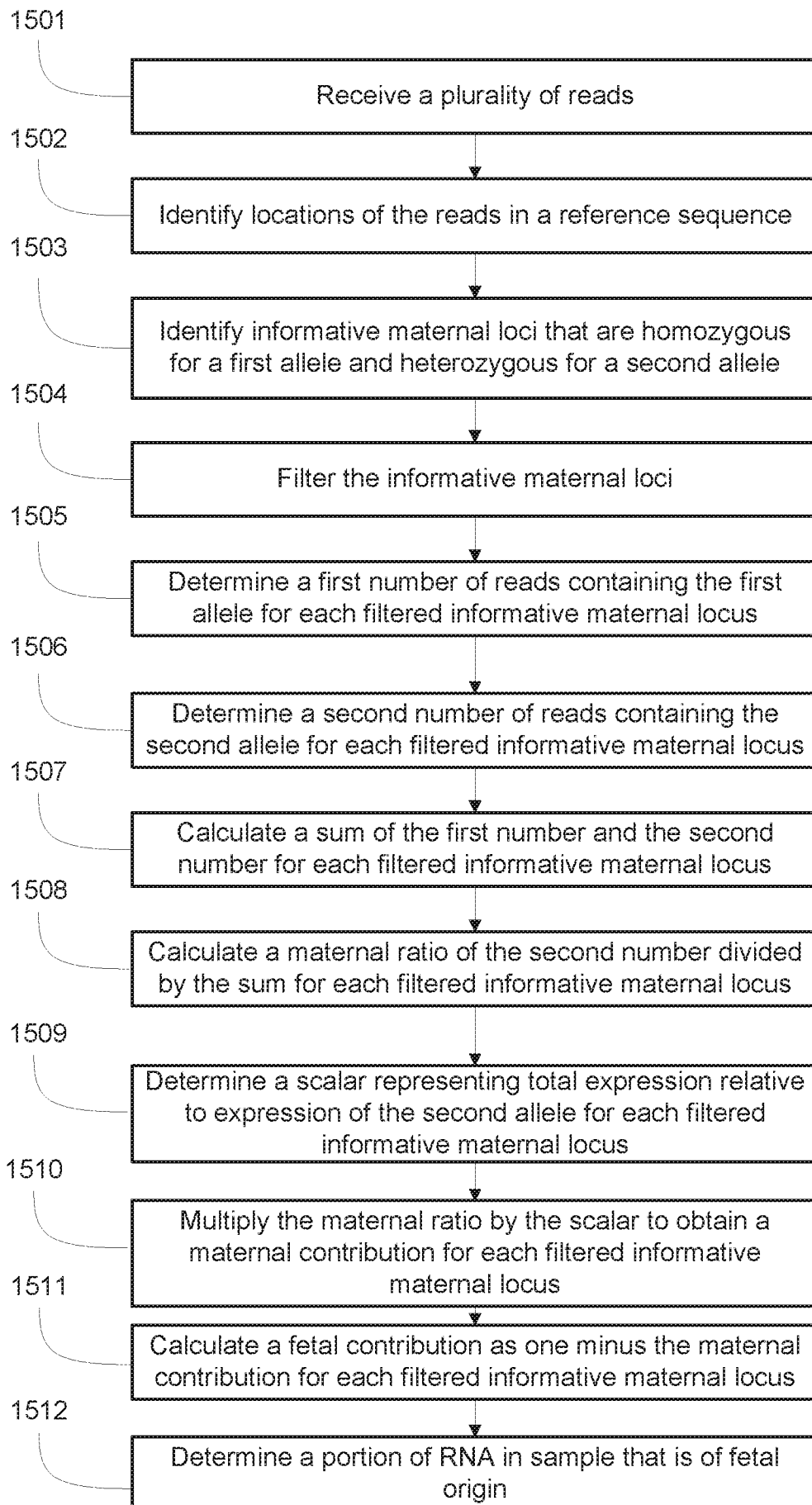


FIG. 15

1500

14/29

|                                                                        | Early pregnancy |                             | Late pregnancy |                |
|------------------------------------------------------------------------|-----------------|-----------------------------|----------------|----------------|
|                                                                        | no. of SNPs     | no. of genes <sup>a</sup>   | no. of SNPs    | no. of genes   |
| <b><i>Fetal-specific SNP alleles<br/>(fetus=AB, mother=AA):</i></b>    |                 |                             |                |                |
| Total informative SNPs/genes                                           | 16,051          | 6,714                       | 20,643         | 7,788          |
| SNPs/genes after ASE filtering                                         | NA <sup>b</sup> |                             | 19,463         | 7,581          |
| Transcripts in maternal plasma                                         | 4,470           | 2,647 (39.43%) <sup>c</sup> | 7,114          | 3,813 (48.96%) |
| Fetal contribution (total)                                             | 109             | 98 (3.70%) <sup>d</sup>     | 504            | 430 (11.28%)   |
| High fetal contribution                                                | 25              | 24 (0.91%) <sup>e</sup>     | 112            | 96 (2.52%)     |
| <b><i>Maternal-specific SNP alleles<br/>(fetus=AA, mother=AB):</i></b> |                 |                             |                |                |
| Total informative SNPs/genes                                           | 15,962          | 6,753                       | 19,833         | 7,761          |
| SNPs/genes after ASE filtering                                         | NA              |                             | 19,343         | 7,656          |
| Transcripts in maternal plasma                                         | 4,414           | 2,654 (39.30%)              | 6,995          | 3,717 (47.89%) |
| Maternal contribution (total)                                          | 3,156           | 2,041 (76.90%)              | 5,023          | 2,911 (78.32%) |
| High maternal contribution                                             | 1,634           | 1,130 (42.58%)              | 3,002          | 1,895 (50.98%) |

a. Number of genes that contained informative SNPs.

b. Allele-specific expression (ASE) filtering was not performed for early pregnancy samples.

c. % of total informative genes that was present in maternal plasma.

d. % of maternal plasma transcripts contributed by fetus.

e. % of maternal plasma transcripts contributed highly by fetus.

FIG. 16

15/29

|                                                                        | Late pregnancy |                             |
|------------------------------------------------------------------------|----------------|-----------------------------|
|                                                                        | no. of SNPs    | no. of genes <sup>a</sup>   |
| <b><i>Fetal-specific SNP alleles<br/>(fetus=AB, mother=AA):</i></b>    |                |                             |
| Total informative SNPs/genes                                           | 20,643         | 7,788                       |
| Transcripts in maternal plasma                                         | 7,303          | 3,839 (49.29%) <sup>b</sup> |
| Fetal contribution (total)                                             | 581            | 485 (12.63%) <sup>c</sup>   |
| High fetal contribution                                                | 132            | 111 (2.89%) <sup>d</sup>    |
| <b><i>Maternal-specific SNP alleles<br/>(fetus=AA, mother=AB):</i></b> |                |                             |
| Total informative SNPs/genes                                           | 19,833         | 7,761                       |
| Transcripts in maternal plasma                                         | 7,365          | 3,829 (49.34%)              |
| Maternal contribution (total)                                          | 5,326          | 3,014 (78.72%)              |
| High maternal contribution                                             | 3,321          | 1,986 (51.87%)              |

a. Number of genes that contained informative SNPs.

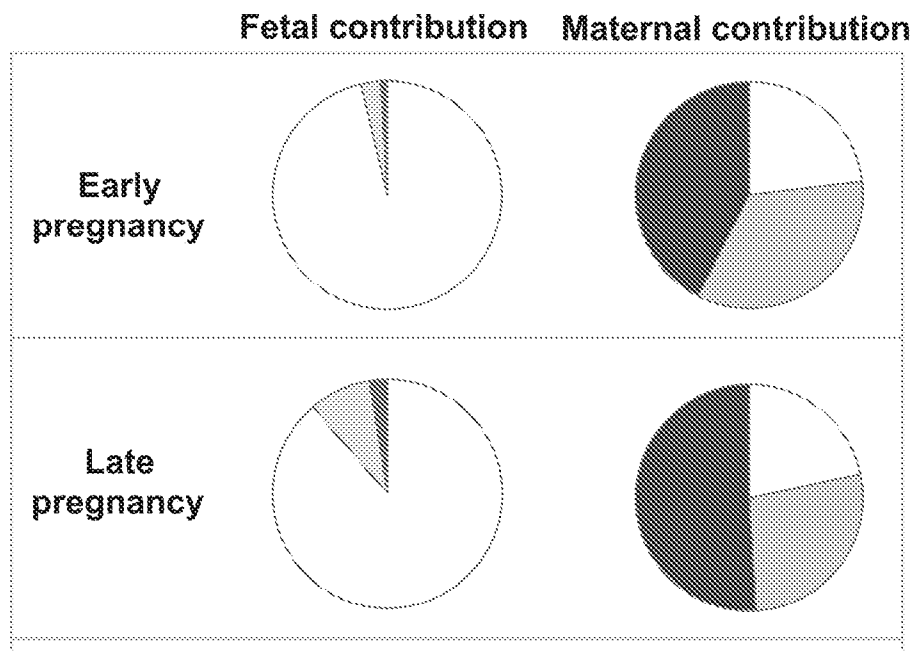
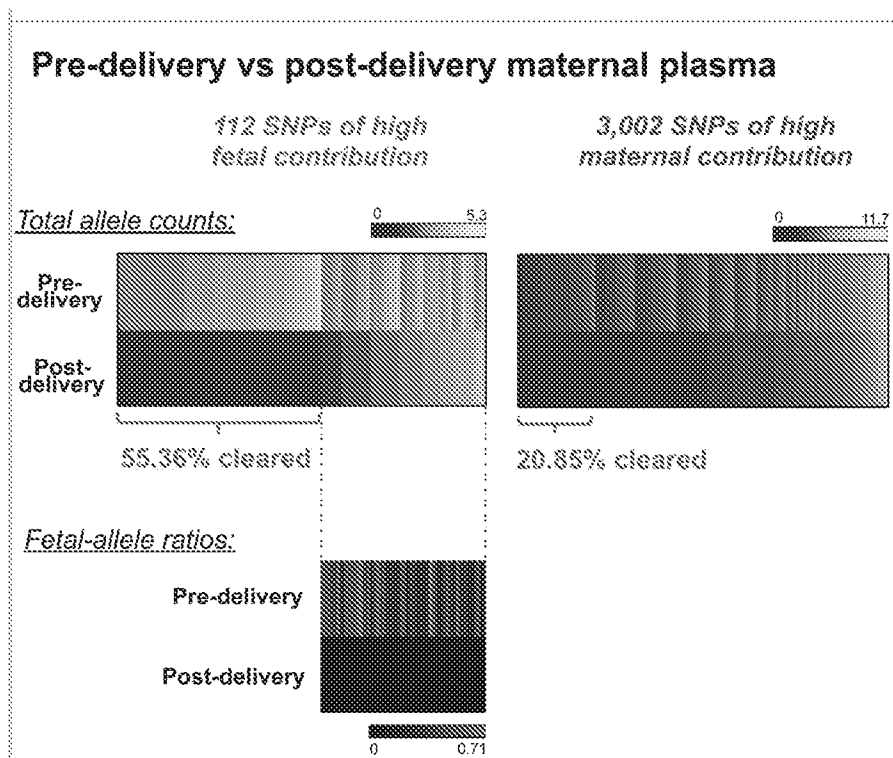
b. % of total informative genes that was present in maternal plasma.

c. % of maternal plasma transcripts contributed by fetus.

d. % of maternal plasma transcripts contributed highly by fetus.

FIG. 17

16/29

**FIG. 18A****FIG. 18B**

17/29

| GNAS (SNP locus: rs7121) | Genotyping            | A-allele count (shared allele) | B-allele count (Maternal-specific) | Fractional maternal contribution, $M = 2 \times \text{Maternal allele} / \text{Maternal} + \text{Fetal allele}$ | Fractional fetal contribution, $F = 1 - M$    | FPKM  |                                                      |
|--------------------------|-----------------------|--------------------------------|------------------------------------|-----------------------------------------------------------------------------------------------------------------|-----------------------------------------------|-------|------------------------------------------------------|
| 7171 (Control)           | Mother: AB, Fetus: AA | 7                              | 6                                  | 0.92                                                                                                            | 0.08                                          | 310.3 |                                                      |
| GNAS (SNP locus: rs7121) | Genotyping            | A-allele count (shared allele) | B-allele count (Fetal-specific)    | Fractional fetal contribution, $F = 2 \times \text{Fetal allele} / \text{Maternal} + \text{Fetal allele}$       | Fractional maternal contribution, $M = 1 - F$ | FPKM  | % change in fractional fetal contribution vs control |
| 5641 (PET)               | Mother: AA, Fetus: AB | 81                             | 4                                  | 0.09                                                                                                            | 0.91                                          | 376.2 | $(0.91 - 0.92) / (0.92) \times 100 = -1.09\%$        |
|                          |                       |                                |                                    |                                                                                                                 |                                               |       | $(0.99 - 0.08) / (0.08) \times 100 = +12.5\%$        |

FIG. 19

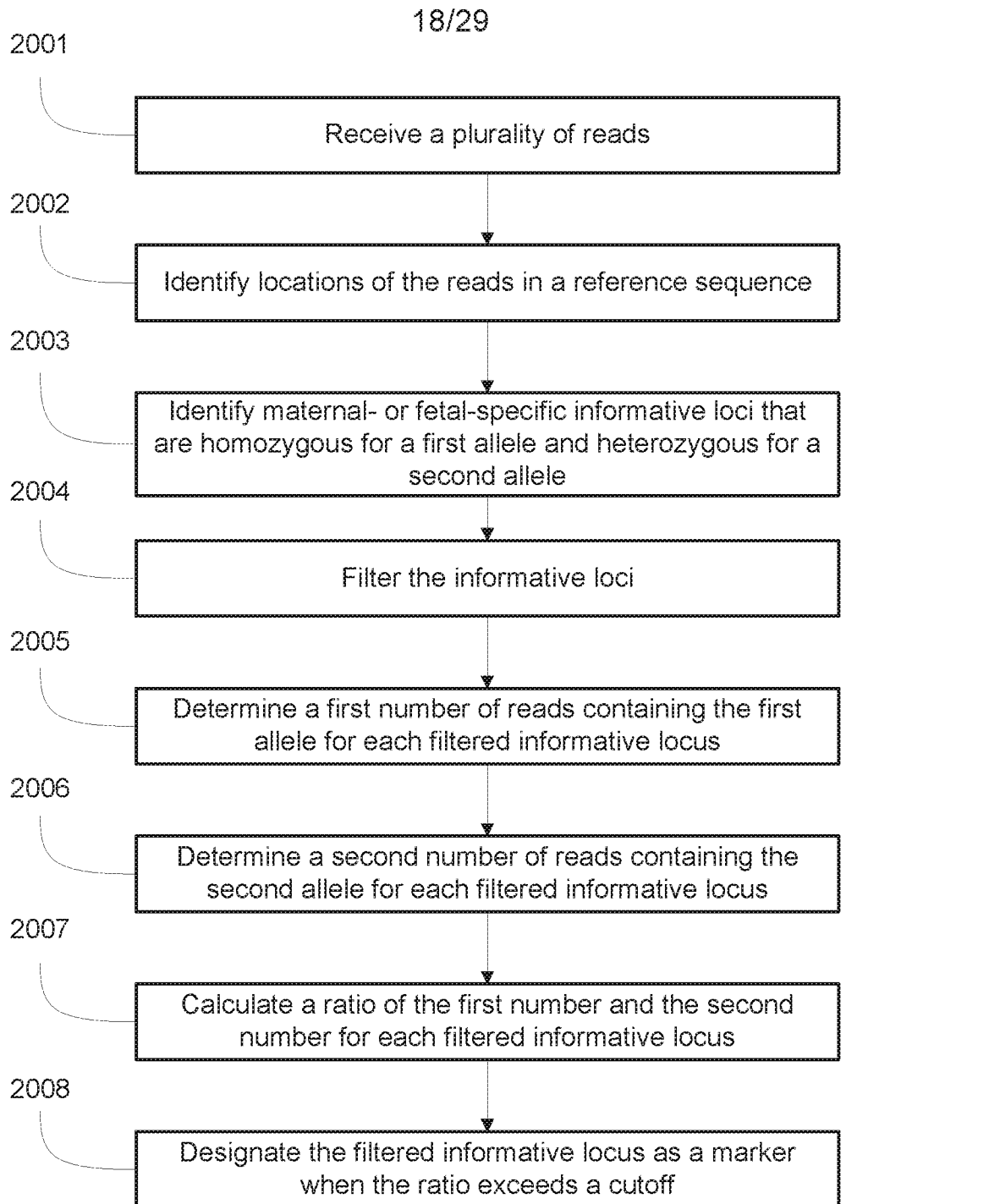


FIG. 20

19/29

| Gene     | Case 9356                              |                                         |             | Case 9415                              |                                         |             | Remark (references) |
|----------|----------------------------------------|-----------------------------------------|-------------|----------------------------------------|-----------------------------------------|-------------|---------------------|
|          | Pre-delivery plasma (transcript level) | Post-delivery plasma (transcript level) | Fold-change | Pre-delivery plasma (transcript level) | Post-delivery plasma (transcript level) | Fold-change |                     |
| CSH1     | 1391.00                                | 17.66                                   | 78.78       | 796.21                                 | 1.13                                    | 704.89      | a (1)               |
| KISS1    | 433.89                                 | 8.25                                    | 52.56       | 147.36                                 | 7.26                                    | 20.29       | a (2)               |
| STAT1    | 227.34                                 | 104.49                                  | 2.18        | 275.22                                 | 85.30                                   | 3.23        | b                   |
| CGA      | 270.02                                 | 6.98                                    | 38.67       | 134.19                                 | 1.00                                    | 134.19      |                     |
| CSH2     | 136.04                                 | 3.89                                    | 34.96       | 185.78                                 | 2.74                                    | 67.84       |                     |
| TFPI2    | 216.09                                 | 15.11                                   | 14.30       | 85.16                                  | 3.55                                    | 24.02       | a (2)               |
| GBP1     | 99.47                                  | 45.89                                   | 2.17        | 153.00                                 | 63.58                                   | 2.41        | b                   |
| PLAC4    | 177.67                                 | 1.03                                    | 172.41      | 69.32                                  | 1.00                                    | 69.32       | a (3)               |
| HSD17B1  | 140.14                                 | 5.94                                    | 23.58       | 93.76                                  | 25.56                                   | 3.67        | b                   |
| CSHL1    | 140.57                                 | 1.00                                    | 140.57      | 66.97                                  | 1.00                                    | 66.97       | a (4)               |
| KRT8     | 86.47                                  | 23.42                                   | 3.69        | 76.78                                  | 13.28                                   | 5.78        | c                   |
| KRT18    | 86.76                                  | 25.92                                   | 3.35        | 64.11                                  | 20.27                                   | 3.16        | b                   |
| HPGD     | 87.76                                  | 38.45                                   | 2.28        | 39.05                                  | 13.36                                   | 2.92        | d                   |
| GADD45G  | 48.82                                  | 20.75                                   | 2.35        | 73.22                                  | 23.37                                   | 3.13        | b                   |
| LGALS14  | 56.55                                  | 1.00                                    | 56.55       | 62.86                                  | 1.00                                    | 62.86       |                     |
| HSD3B1   | 60.62                                  | 3.51                                    | 17.28       | 48.26                                  | 1.00                                    | 48.26       |                     |
| KRT19    | 77.95                                  | 24.04                                   | 3.24        | 30.71                                  | 3.52                                    | 8.71        |                     |
| SERPINE1 | 37.39                                  | 15.29                                   | 2.45        | 60.90                                  | 12.71                                   | 4.79        | a (5)               |
| GDF15    | 62.32                                  | 3.68                                    | 16.92       | 33.52                                  | 12.10                                   | 2.77        |                     |
| CYP19A1  | 70.84                                  | 4.90                                    | 14.47       | 18.65                                  | 1.00                                    | 18.65       |                     |
| PSG4     | 36.10                                  | 1.45                                    | 24.89       | 47.82                                  | 1.00                                    | 47.82       |                     |
| PSG3     | 53.00                                  | 1.00                                    | 53.00       | 23.03                                  | 1.00                                    | 23.03       |                     |
| CRYAB    | 15.46                                  | 1.00                                    | 15.46       | 58.22                                  | 4.50                                    | 12.93       |                     |
| HSPB8    | 35.57                                  | 6.62                                    | 5.37        | 36.79                                  | 13.47                                   | 2.73        |                     |
| PKIB     | 45.08                                  | 8.79                                    | 5.13        | 26.12                                  | 8.09                                    | 3.23        |                     |
| PGF      | 44.72                                  | 5.40                                    | 8.29        | 24.94                                  | 3.80                                    | 6.57        |                     |
| CYP11A1  | 40.77                                  | 3.64                                    | 11.20       | 28.04                                  | 1.71                                    | 16.41       |                     |
| PSG5     | 42.56                                  | 1.00                                    | 42.56       | 25.66                                  | 1.00                                    | 25.66       |                     |
| PSG1     | 37.70                                  | 1.49                                    | 25.29       | 28.17                                  | 1.00                                    | 28.17       |                     |
| PAPPA    | 40.90                                  | 5.91                                    | 6.92        | 20.03                                  | 1.00                                    | 20.03       | a (6)               |
| ADAM12   | 44.48                                  | 4.01                                    | 11.09       | 15.16                                  | 1.00                                    | 15.16       | a (7)               |
| PSG2     | 29.16                                  | 1.00                                    | 29.16       | 29.95                                  | 1.00                                    | 29.95       |                     |
| VGLL3    | 34.80                                  | 1.98                                    | 17.54       | 20.36                                  | 1.80                                    | 11.34       |                     |
| KRT7     | 27.20                                  | 10.39                                   | 2.62        | 26.54                                  | 9.75                                    | 2.72        |                     |
| TMEM54   | 32.99                                  | 5.94                                    | 5.56        | 18.70                                  | 5.22                                    | 3.58        |                     |
| PRKCZ    | 28.22                                  | 10.05                                   | 2.81        | 23.12                                  | 8.76                                    | 2.64        |                     |
| SDC1     | 30.62                                  | 2.62                                    | 11.68       | 17.43                                  | 1.84                                    | 9.45        |                     |
| LGALS13  | 32.32                                  | 1.00                                    | 32.32       | 15.60                                  | 1.00                                    | 15.60       |                     |
| EFHD1    | 15.55                                  | 2.80                                    | 5.56        | 30.55                                  | 3.94                                    | 7.76        |                     |
| CAPN6    | 23.18                                  | 1.64                                    | 14.14       | 22.90                                  | 1.00                                    | 22.90       |                     |
| XAGE3    | 25.08                                  | 2.59                                    | 9.67        | 13.08                                  | 1.00                                    | 13.08       |                     |
| EBI3     | 18.79                                  | 6.48                                    | 2.90        | 17.96                                  | 7.39                                    | 2.46        |                     |
| GH2      | 19.16                                  | 1.00                                    | 19.16       | 17.22                                  | 1.00                                    | 17.22       | a (7)               |
| PAGE4    | 28.89                                  | 2.99                                    | 9.67        | 6.28                                   | 1.00                                    | 6.28        |                     |

FIG. 21

20/29

| Gene         | Case 9356                              |                                         |             | Case 9415                              |                                         |             | Remark (references) |
|--------------|----------------------------------------|-----------------------------------------|-------------|----------------------------------------|-----------------------------------------|-------------|---------------------|
|              | Pre-delivery plasma (transcript level) | Post-delivery plasma (transcript level) | Fold-change | Pre-delivery plasma (transcript level) | Post-delivery plasma (transcript level) | Fold-change |                     |
| ALPP         | 19.62                                  | 1.54                                    | 12.73       | 14.03                                  | 1.00                                    | 14.03       |                     |
| INHBA        | 18.99                                  | 2.71                                    | 7.01        | 14.51                                  | 4.29                                    | 3.38        | a (6)               |
| LOC100505658 | 17.53                                  | 1.00                                    | 17.53       | 15.65                                  | 1.00                                    | 15.65       |                     |
| FBLN1        | 10.12                                  | 2.12                                    | 4.76        | 20.01                                  | 1.28                                    | 15.62       |                     |
| SEMA3B       | 16.06                                  | 2.52                                    | 6.38        | 12.90                                  | 1.00                                    | 12.90       |                     |
| GPC3         | 18.22                                  | 1.00                                    | 18.22       | 10.12                                  | 1.00                                    | 10.12       |                     |
| PLAC2        | 19.86                                  | 1.99                                    | 9.96        | 8.04                                   | 1.97                                    | 4.09        |                     |
| PSG9         | 7.10                                   | 1.00                                    | 7.10        | 20.32                                  | 1.00                                    | 20.32       | a (8)               |
| FN1          | 17.30                                  | 6.57                                    | 2.63        | 9.72                                   | 3.81                                    | 2.55        |                     |
| NOS3         | 10.01                                  | 3.45                                    | 2.90        | 16.07                                  | 7.08                                    | 2.27        |                     |
| LOC100506655 | 12.29                                  | 1.00                                    | 12.29       | 13.53                                  | 1.00                                    | 13.53       |                     |
| PSG11        | 19.48                                  | 1.83                                    | 10.63       | 5.77                                   | 1.00                                    | 5.77        |                     |
| SPTLC3       | 19.82                                  | 1.00                                    | 19.82       | 4.99                                   | 1.00                                    | 4.99        |                     |
| EXPH5        | 12.58                                  | 4.48                                    | 2.81        | 12.09                                  | 2.24                                    | 5.40        |                     |
| HSPA2        | 12.86                                  | 5.85                                    | 2.20        | 11.40                                  | 4.87                                    | 2.34        |                     |
| PSG6         | 10.66                                  | 1.00                                    | 10.66       | 13.38                                  | 1.00                                    | 13.38       |                     |
| PLAC1        | 17.08                                  | 1.00                                    | 17.08       | 6.60                                   | 1.00                                    | 6.60        | a (3)               |
| TACC2        | 5.93                                   | 1.61                                    | 3.69        | 16.24                                  | 1.64                                    | 9.89        |                     |
| PRPF40B      | 8.27                                   | 3.98                                    | 2.08        | 12.53                                  | 5.32                                    | 2.36        |                     |
| LOC388948    | 12.97                                  | 1.00                                    | 12.97       | 7.71                                   | 1.00                                    | 7.71        |                     |
| SERPINB2     | 13.48                                  | 1.36                                    | 9.91        | 6.66                                   | 1.44                                    | 4.77        | a (9)               |
| CRH          | 15.40                                  | 1.00                                    | 15.40       | 4.75                                   | 1.00                                    | 4.75        | a (10)              |
| GBP1P1       | 6.35                                   | 1.19                                    | 5.32        | 13.04                                  | 5.04                                    | 2.59        |                     |
| CLDN4        | 12.50                                  | 1.00                                    | 12.50       | 6.45                                   | 2.84                                    | 2.27        |                     |
| C2orf72      | 11.14                                  | 3.29                                    | 3.38        | 7.26                                   | 1.74                                    | 4.18        |                     |
| PAPPA2       | 10.92                                  | 1.53                                    | 7.13        | 7.48                                   | 1.00                                    | 7.48        |                     |
| HIST2H3A     | 14.75                                  | 7.27                                    | 2.03        | 2.44                                   | 1.02                                    | 2.39        |                     |
| HIST2H3C     | 14.75                                  | 7.27                                    | 2.03        | 2.44                                   | 1.02                                    | 2.39        |                     |
| TCL6         | 12.92                                  | 1.00                                    | 12.92       | 3.93                                   | 1.00                                    | 3.93        |                     |
| MFSD2A       | 8.09                                   | 3.35                                    | 2.42        | 8.72                                   | 1.00                                    | 8.72        |                     |
| ZFAT-AS1     | 9.10                                   | 3.14                                    | 2.90        | 7.25                                   | 3.31                                    | 2.19        |                     |
| INSL4        | 13.90                                  | 2.40                                    | 5.80        | 2.01                                   | 1.00                                    | 2.01        |                     |
| DHRS2        | 12.24                                  | 6.11                                    | 2.00        | 3.30                                   | 1.00                                    | 3.30        |                     |
| HES2         | 11.03                                  | 3.11                                    | 3.54        | 4.50                                   | 1.46                                    | 3.08        |                     |
| WLS          | 11.06                                  | 4.77                                    | 2.32        | 4.40                                   | 1.68                                    | 2.63        |                     |
| PLCXD3       | 10.49                                  | 3.62                                    | 2.90        | 4.88                                   | 2.01                                    | 2.43        |                     |
| LOC100505483 | 5.40                                   | 1.00                                    | 5.40        | 9.39                                   | 2.62                                    | 3.58        |                     |
| C1orf130     | 11.60                                  | 1.85                                    | 6.28        | 2.48                                   | 1.00                                    | 2.48        |                     |
| FOSB         | 3.02                                   | 1.00                                    | 3.02        | 10.65                                  | 4.94                                    | 2.16        |                     |
| GCM1         | 5.93                                   | 1.60                                    | 3.71        | 6.94                                   | 1.00                                    | 6.94        | a (8)               |
| TRPV6        | 9.31                                   | 1.00                                    | 9.31        | 3.41                                   | 1.00                                    | 3.41        |                     |
| TFAP2A       | 4.02                                   | 1.00                                    | 4.02        | 8.59                                   | 1.46                                    | 5.87        |                     |
| MMP11        | 10.08                                  | 1.96                                    | 5.16        | 2.46                                   | 1.00                                    | 2.46        |                     |
| TUSC3        | 9.90                                   | 2.66                                    | 3.73        | 2.55                                   | 1.00                                    | 2.55        |                     |
| HMOX1        | 7.15                                   | 2.25                                    | 3.18        | 5.13                                   | 2.26                                    | 2.27        |                     |

FIG. 21 cont.

21/29

| Gene         | Case 9356                              |                                         |             | Case 9415                              |                                         |             | Remark (references) |
|--------------|----------------------------------------|-----------------------------------------|-------------|----------------------------------------|-----------------------------------------|-------------|---------------------|
|              | Pre-delivery plasma (transcript level) | Post-delivery plasma (transcript level) | Fold-change | Pre-delivery plasma (transcript level) | Post-delivery plasma (transcript level) | Fold-change |                     |
| CCK          | 7.06                                   | 1.00                                    | 7.06        | 4.98                                   | 1.00                                    | 4.98        |                     |
| LOC100129938 | 8.56                                   | 1.61                                    | 5.32        | 3.38                                   | 1.00                                    | 3.38        |                     |
| C8orf39      | 4.02                                   | 1.00                                    | 4.02        | 7.86                                   | 2.93                                    | 2.69        |                     |
| GLDN         | 9.39                                   | 1.00                                    | 9.39        | 2.44                                   | 1.00                                    | 2.44        |                     |
| PGAP3        | 6.10                                   | 2.19                                    | 2.78        | 4.84                                   | 2.32                                    | 2.09        |                     |
| MSX2P1       | 3.63                                   | 1.00                                    | 3.63        | 6.87                                   | 3.36                                    | 2.05        |                     |
| GH1          | 4.33                                   | 1.00                                    | 4.33        | 6.02                                   | 1.00                                    | 6.02        |                     |
| SVEP1        | 7.79                                   | 2.98                                    | 2.61        | 2.26                                   | 1.00                                    | 2.26        |                     |
| PPP1R32      | 2.78                                   | 1.00                                    | 2.78        | 7.24                                   | 1.35                                    | 5.37        |                     |
| PSG8         | 5.01                                   | 1.00                                    | 5.01        | 4.94                                   | 1.00                                    | 4.94        |                     |
| ENDOU        | 7.24                                   | 2.40                                    | 3.02        | 2.27                                   | 1.00                                    | 2.27        |                     |
| EGFR         | 6.83                                   | 1.00                                    | 6.83        | 2.54                                   | 1.00                                    | 2.54        |                     |
| DUSP4        | 5.24                                   | 1.61                                    | 3.26        | 4.13                                   | 1.41                                    | 2.92        |                     |
| PHYHPL       | 5.53                                   | 1.00                                    | 5.53        | 3.48                                   | 1.39                                    | 2.51        |                     |
| CTSF         | 6.01                                   | 1.00                                    | 6.01        | 2.77                                   | 1.03                                    | 2.69        |                     |
| TRIM29       | 3.54                                   | 1.00                                    | 3.54        | 5.13                                   | 1.00                                    | 5.13        |                     |
| RCN3         | 3.07                                   | 1.00                                    | 3.07        | 5.34                                   | 1.12                                    | 4.77        |                     |
| SPRE2        | 5.93                                   | 2.27                                    | 2.61        | 2.48                                   | 1.00                                    | 2.48        |                     |
| LOC100216007 | 4.60                                   | 1.06                                    | 4.35        | 3.55                                   | 1.49                                    | 2.39        |                     |
| FAM176A      | 5.76                                   | 2.10                                    | 2.74        | 2.36                                   | 1.00                                    | 2.36        |                     |
| SCIN         | 5.18                                   | 1.00                                    | 5.18        | 2.82                                   | 1.00                                    | 2.82        |                     |
| ZNF500       | 2.41                                   | 1.00                                    | 2.41        | 5.52                                   | 2.23                                    | 2.47        |                     |
| PRR16        | 2.83                                   | 1.00                                    | 2.83        | 4.91                                   | 1.18                                    | 4.18        |                     |
| LOC100128054 | 4.55                                   | 1.05                                    | 4.35        | 3.08                                   | 1.00                                    | 3.08        |                     |
| OLR1         | 4.53                                   | 1.17                                    | 3.87        | 2.71                                   | 1.00                                    | 2.71        |                     |
| SLC30A2      | 5.18                                   | 1.00                                    | 5.18        | 2.00                                   | 1.00                                    | 2.00        |                     |
| LOC285972    | 3.49                                   | 1.00                                    | 3.49        | 3.64                                   | 1.02                                    | 3.58        |                     |
| HESX1        | 4.25                                   | 1.26                                    | 3.38        | 2.64                                   | 1.00                                    | 2.64        |                     |
| TMEM139      | 4.61                                   | 1.00                                    | 4.61        | 2.25                                   | 1.00                                    | 2.25        |                     |
| ZNF727       | 3.82                                   | 1.00                                    | 3.82        | 2.58                                   | 1.24                                    | 2.09        |                     |
| TM4SF19      | 4.04                                   | 1.39                                    | 2.90        | 2.34                                   | 1.00                                    | 2.34        |                     |
| EFS          | 3.88                                   | 1.00                                    | 3.88        | 2.38                                   | 1.00                                    | 2.38        |                     |
| TMD4         | 2.08                                   | 1.00                                    | 2.08        | 3.62                                   | 1.51                                    | 2.39        |                     |
| ALDH3B2      | 2.91                                   | 1.00                                    | 2.91        | 2.76                                   | 1.00                                    | 2.76        |                     |
| KRT81        | 2.61                                   | 1.00                                    | 2.61        | 2.92                                   | 1.00                                    | 2.92        |                     |
| MUC15        | 2.94                                   | 1.00                                    | 2.94        | 2.19                                   | 1.00                                    | 2.19        |                     |
| PRSS8        | 2.20                                   | 1.00                                    | 2.20        | 2.87                                   | 1.00                                    | 2.87        |                     |
| SH2D5        | 2.41                                   | 1.00                                    | 2.41        | 2.42                                   | 1.00                                    | 2.42        |                     |
| LOC728175    | 2.28                                   | 1.00                                    | 2.28        | 2.31                                   | 1.10                                    | 2.09        |                     |
| GRHL2        | 2.45                                   | 1.00                                    | 2.45        | 2.13                                   | 1.00                                    | 2.13        |                     |
| PABPN1L      | 2.18                                   | 1.00                                    | 2.18        | 2.37                                   | 1.00                                    | 2.37        |                     |
| CORO6        | 2.08                                   | 1.00                                    | 2.08        | 2.07                                   | 1.00                                    | 2.07        |                     |

**Remark:**

- a. Transcripts previously reported to be pregnancy-associated in maternal plasma
- b. Transcripts newly identified in this study by maternal plasma RNA-seq and validated by real-time RT-PCR (Supplemental Data Fig. 6)
- c. *KRT8* mRNA was not studied by real-time RT-PCR as the detection assay cannot be designed
- d. Real-time RT-PCR result showed that maternal plasma *HPGD* mRNA did not show clearance pattern after delivery (Supplemental Data Fig. 6)

**References:**

- Ng EKO, Tsui NBY, Lau TK, Leung TN, Chiu RWK, Panesar NS, et al. Proc Natl Acad Sci U S A 2003;100:4748-53.
- Tsui NBY, Chim SSC, Chiu RWK, Lau TK, Ng EKO, Leung TN, et al. J Med Genet 2004;41:461-7.
- Lo YMD, Tsui NBY, Chiu RWK, Lau TK, Leung TN, Heung MMS, et al. Nat Med 2007;13:218-23.
- Heung MMS, Jin S, Tsui NBY, Ding C, Leung TY, Lau TK, et al. PLoS One 2009;4:e5858.
- Purwosunu Y, Sekizawa A, Koide K, Farina A, Wibowo N, Wiknjosastro GH, et al. Clin Chem 2007;53:399-404.
- Wong BCK, Chiu RWK, Tsui NBY, Chan KCA, Chan LW, Lau TK, et al. Clin Chem 2005;51:1788-95.
- Pang WWI, Tsui MHY, Sahota D, Leung TY, Lau TK, Lo YMD, Chiu RWK. Prenat Diagn 2009;29:495-504.
- Go AT, Visser A, Mulders MA, Blankenstein MA, Van Vugt JM, Oudejans CB. Clin Chem 2004;50:1413-4.
- Tsui NBY, Wong BCK, Leung TY, Lau TK, Chiu RWK, Lo YMD. Prenat Diagn 2009;29:1031-7.
- Ng EKO, Leung TN, Tsui NBY, Lau TK, Panesar NS, Chiu RWK, Lo YMD. Clin Chem 2003;49:727-31.

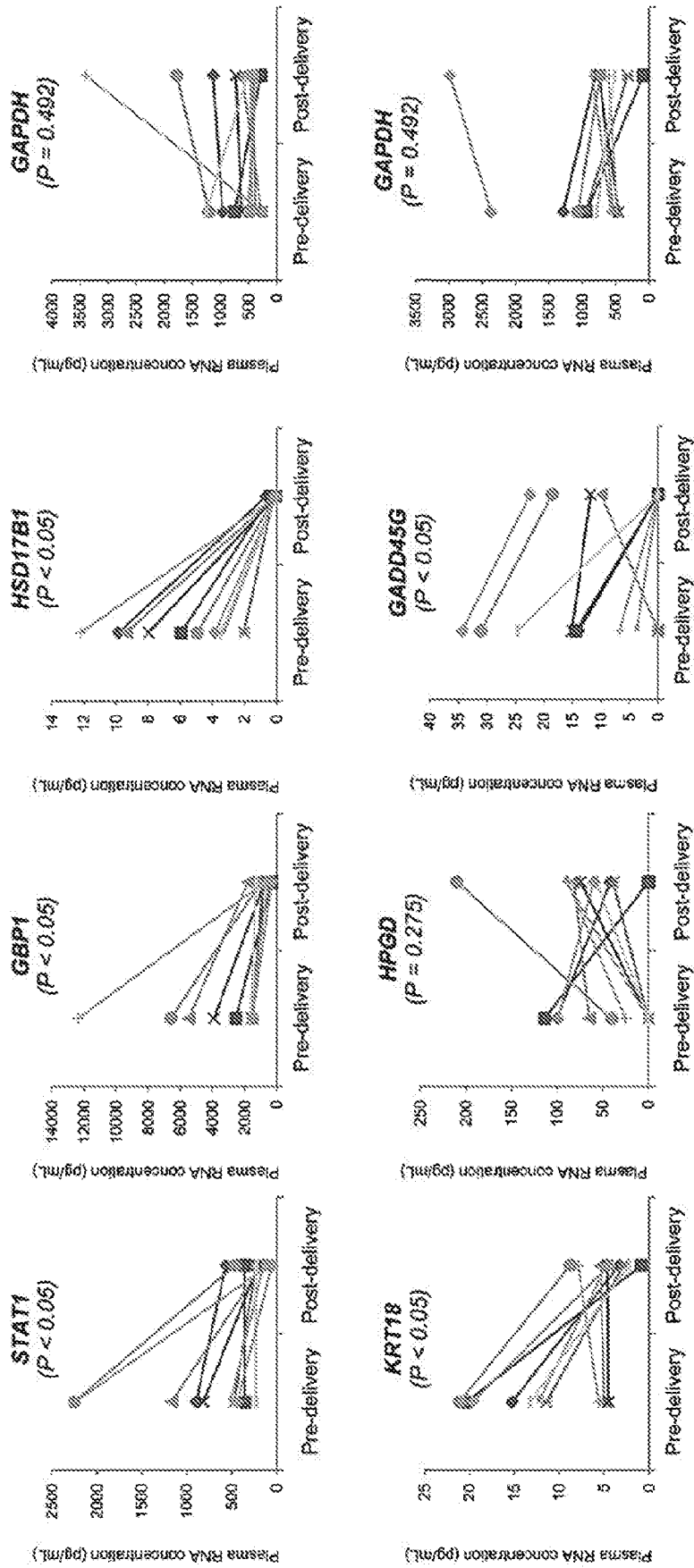


FIG. 22

23/29

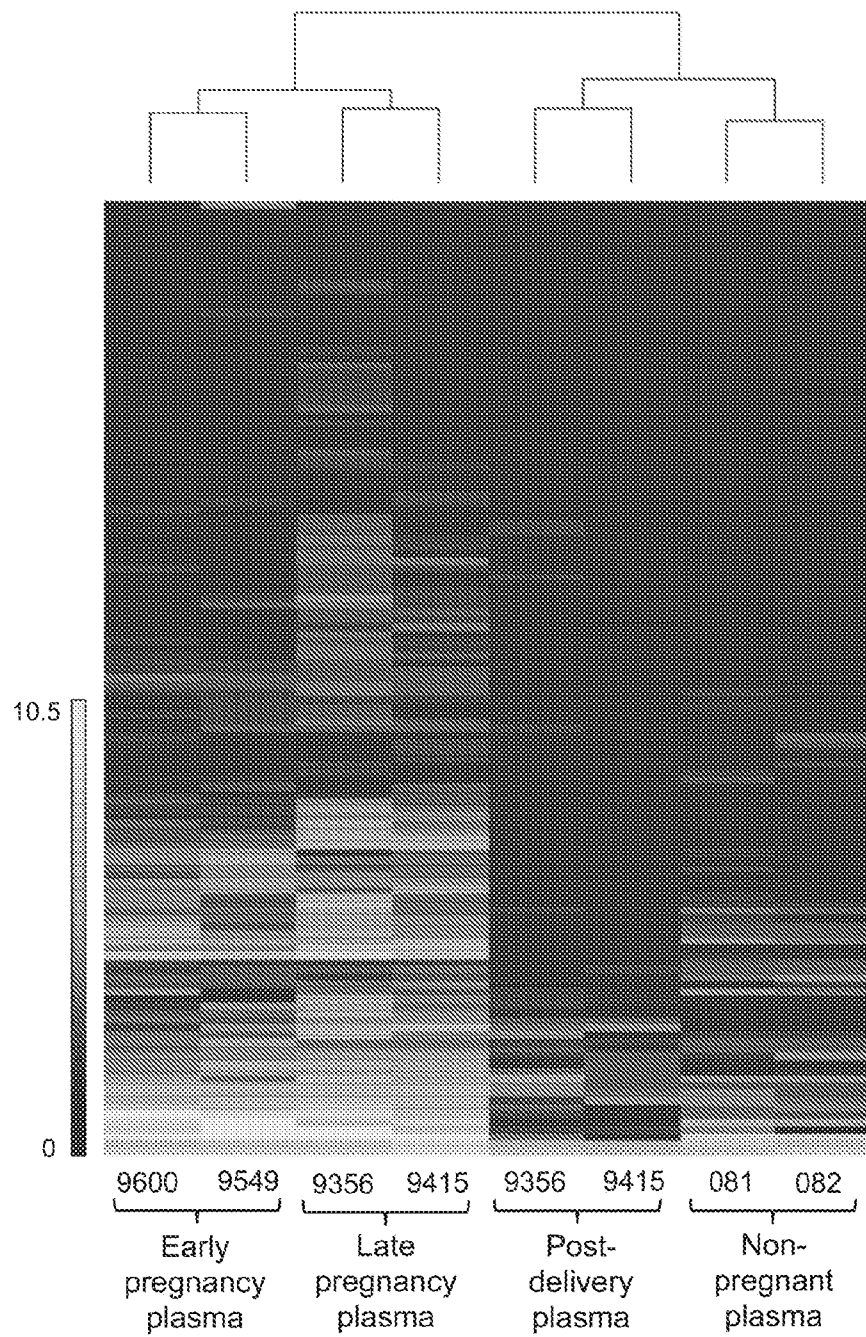


FIG. 23

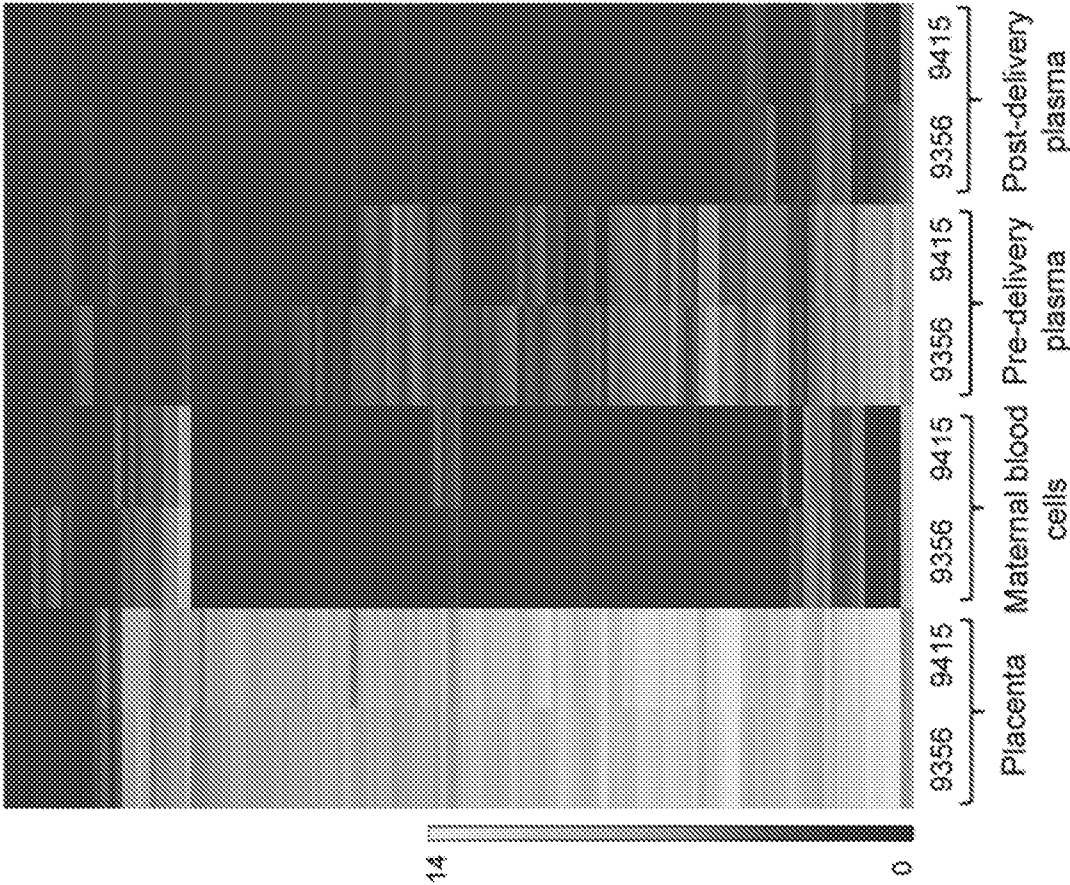


FIG. 24A

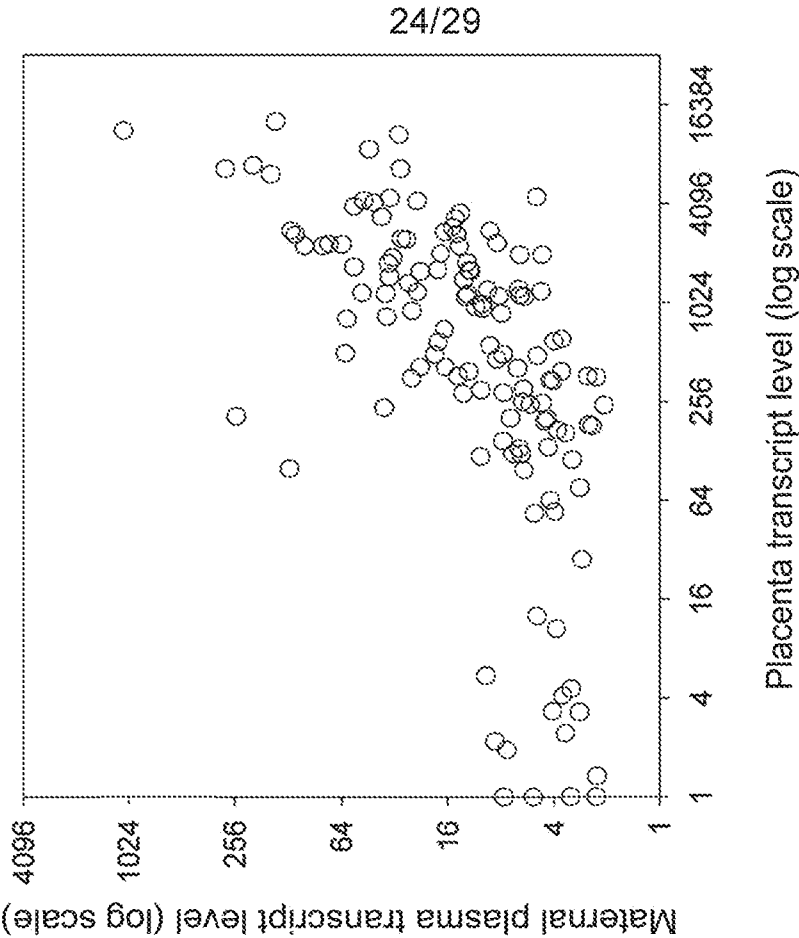


FIG. 24B

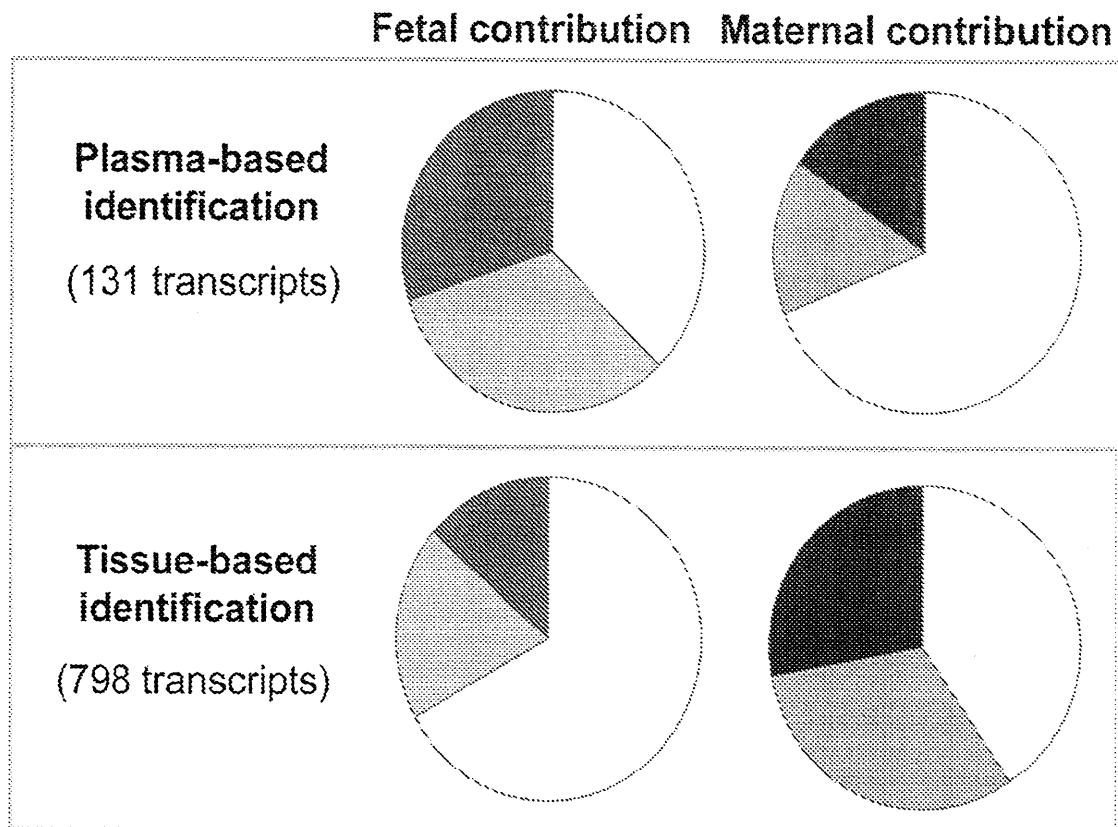


**FIG. 25**

26/29

| RNAs          | Preeclampsia | Normal | RNAs     | Preeclampsia | Normal |
|---------------|--------------|--------|----------|--------------|--------|
| ADAM9         | 26.78        | 11.26  | LY6E     | 84.52        | 31.38  |
| AGBL5         | 144.47       | 65.14  | MEIS1    | 79.49        | 18.77  |
| APOBR         | 64.12        | 26.31  | MLH3     | 150.61       | 36.10  |
| APOL2         | 59.24        | 29.05  | MYADM    | 51.11        | 16.60  |
| APP           | 212.58       | 84.93  | NCF1     | 107.35       | 41.90  |
| ASAH1         | 167.14       | 47.38  | NCF1B    | 34.80        | 9.41   |
| ATP5I         | 23.85        | 9.20   | NDUFA1   | 20.73        | 7.36   |
| ATP6V0E1      | 60.73        | 20.56  | NES      | 176.78       | 58.83  |
| B2M           | 1765.75      | 654.19 | NFAM1    | 49.17        | 17.91  |
| BCAP31        | 42.85        | 14.86  | NGFRAP1  | 106.72       | 19.52  |
| BRK1          | 91.46        | 41.63  | NPTN     | 80.63        | 29.97  |
| C12orf76      | 16.97        | 4.56   | NT5C3    | 173.39       | 65.34  |
| C19orf59      | 22.94        | 6.42   | OST4     | 404.86       | 100.63 |
| C19orf79      | 13.22        | 3.00   | PARK7    | 97.39        | 40.79  |
| C1orf151-NBL1 | 25.89        | 11.19  | PARP10   | 52.41        | 19.75  |
| C21orf7       | 308.80       | 83.41  | PDGFA    | 55.19        | 24.29  |
| C7orf53       | 8.04         | 0.73   | PF4      | 680.43       | 208.45 |
| CARD16        | 85.90        | 29.13  | PGRMC1   | 332.76       | 78.90  |
| CD97          | 59.09        | 28.74  | PRIC285  | 72.34        | 20.44  |
| CEBPD         | 147.37       | 44.30  | PSMB9    | 73.17        | 34.36  |
| CTSA          | 341.67       | 138.37 | RAB32    | 51.90        | 25.20  |
| CYB5R1        | 25.14        | 10.12  | RABAC1   | 25.10        | 7.80   |
| DDX11L10      | 38.97        | 7.34   | RBX1     | 36.44        | 15.06  |
| DUSP1         | 168.06       | 30.57  | RNF213   | 316.69       | 147.00 |
| DYNLRB1       | 166.30       | 59.63  | RPPH1    | 242.37       | 63.73  |
| EMP3          | 99.80        | 39.75  | S100P    | 48.92        | 14.31  |
| ENKUR         | 64.87        | 15.45  | S1PR3    | 9.45         | 1.41   |
| GALM          | 31.68        | 5.09   | SAT1     | 213.55       | 100.86 |
| GDI1          | 91.22        | 41.05  | SEPT3    | 14.54        | 6.35   |
| HIST1H2AC     | 271.60       | 72.77  | SERF2    | 310.66       | 144.79 |
| HIST1H3H      | 131.91       | 40.96  | SHISA5   | 141.53       | 59.85  |
| HIST1H4A      | 20.40        | 5.53   | SIGLEC1  | 18.55        | 3.32   |
| HIST1H4B      | 25.44        | 5.58   | SIGLEC14 | 10.79        | 0.95   |
| HIST1H4E      | 74.16        | 26.59  | SNN      | 348.09       | 171.73 |
| HIST1H4H      | 69.35        | 18.31  | SOD2     | 569.41       | 229.85 |
| HIST1H4L      | 20.99        | 6.89   | SPARC    | 914.92       | 286.17 |
| HLA-C         | 417.81       | 203.10 | TIMP1    | 76.27        | 27.68  |
| HLA-L         | 11.78        | 3.90   | TMEM140  | 121.93       | 29.08  |
| HRC           | 14.87        | 0.16   | TMEM185A | 36.93        | 12.09  |
| HSPA1A        | 37.29        | 14.90  | TMEM50A  | 139.68       | 32.72  |
| IFI6          | 171.27       | 18.29  | TRIM22   | 135.78       | 58.79  |
| ISG20         | 86.19        | 23.09  | TSC22D3  | 330.23       | 108.27 |
| JAM3          | 121.57       | 52.31  | UBE2L6   | 171.88       | 63.40  |
| KLF6          | 127.12       | 62.64  | VKORC1L1 | 63.06        | 25.17  |
| LEPR          | 43.19        | 17.71  | VTRNA1-1 | 7.23         | 0.08   |
| LEPROT        | 70.13        | 34.38  | YIF1B    | 36.33        | 16.96  |
| LILRA5        | 31.45        | 11.05  | YPEL3    | 150.75       | 73.23  |
| LOC146336     | 13.75        | 4.89   | YWHAH    | 236.85       | 116.18 |
| LRRC32        | 102.05       | 34.23  | ZNF485   | 15.35        | 6.38   |

FIG. 26

| PAPPA<br>SNP rsID | DNA genotype |        | Placenta |      | Maternal<br>blood cells |   |    | Pre-delivery<br>maternal plasma |   | Post-delivery<br>maternal plasma |   |
|-------------------|--------------|--------|----------|------|-------------------------|---|----|---------------------------------|---|----------------------------------|---|
|                   | Fetus        | Mother | A        | G    | A                       | G | A  | A                               | G | A                                | G |
| rs386088          | GA           | AA     | 2421     | 2164 | 0                       | 0 | 16 | 21                              | 0 | 0                                | 0 |

FIG. 27

27/29

| H19<br>SNP rsID        | DNA genotype |        | Placenta    |                   | Maternal<br>blood cells |                   | Pre-delivery<br>maternal plasma |                   | Post-delivery<br>maternal plasma |                   |
|------------------------|--------------|--------|-------------|-------------------|-------------------------|-------------------|---------------------------------|-------------------|----------------------------------|-------------------|
|                        | Fetus        | Mother | Shared      | Maternal-specific | Shared                  | Maternal-specific | Shared                          | Maternal-specific | Shared                           | Maternal-specific |
| rs2839698 <sup>a</sup> | AA           | AG     | 3418<br>(A) | 10<br>(G)         | 0<br>(A)                | 0<br>(G)          | 246<br>(A)                      | 1679<br>(G)       | 0<br>(A)                         | 808<br>(G)        |
| rs2839701              | GG           | CG     | 4959<br>(G) | 8<br>(C)          | 0<br>(G)                | 0<br>(C)          | 33<br>(G)                       | 219<br>(C)        | 1<br>(G)                         | 78<br>(C)         |
| rs2839702              | CC           | AC     | 4996<br>(C) | 8<br>(A)          | 0<br>(C)                | 0<br>(A)          | 38<br>(C)                       | 233<br>(A)        | 2<br>(C)                         | 92<br>(A)         |
| rs3741219              | GG           | AG     | 2255<br>(G) | 15<br>(A)         | 0<br>(G)                | 0<br>(A)          | 17<br>(G)                       | 158<br>(A)        | 0<br>(G)                         | 96<br>(A)         |

a: The shared A-allele was imprinted while the maternal-specific G-allele was transcribed. Details of the methylation status are shown in Supplemental Data Fig. 5.

FIG. 28

28/29

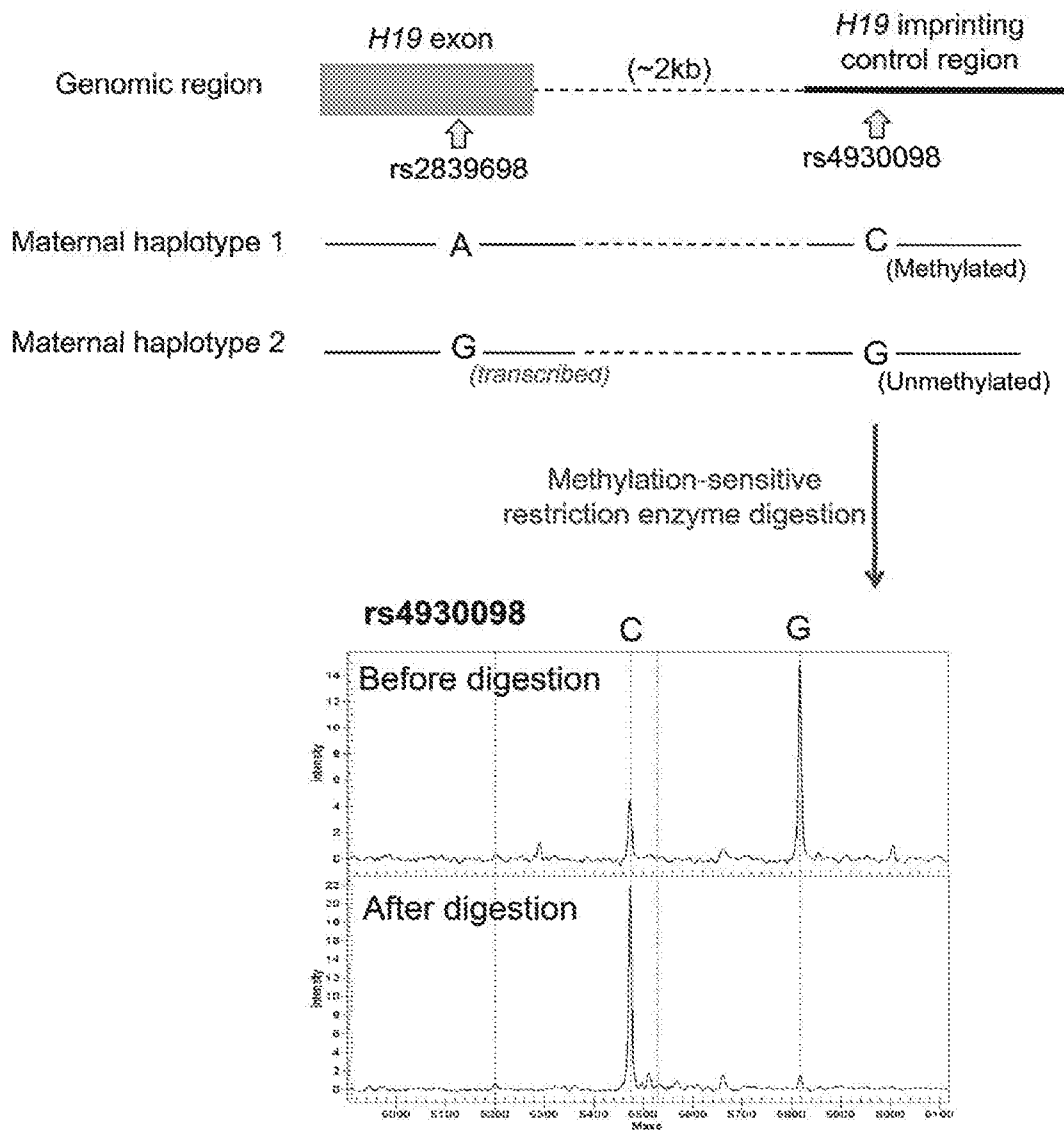


FIG. 29

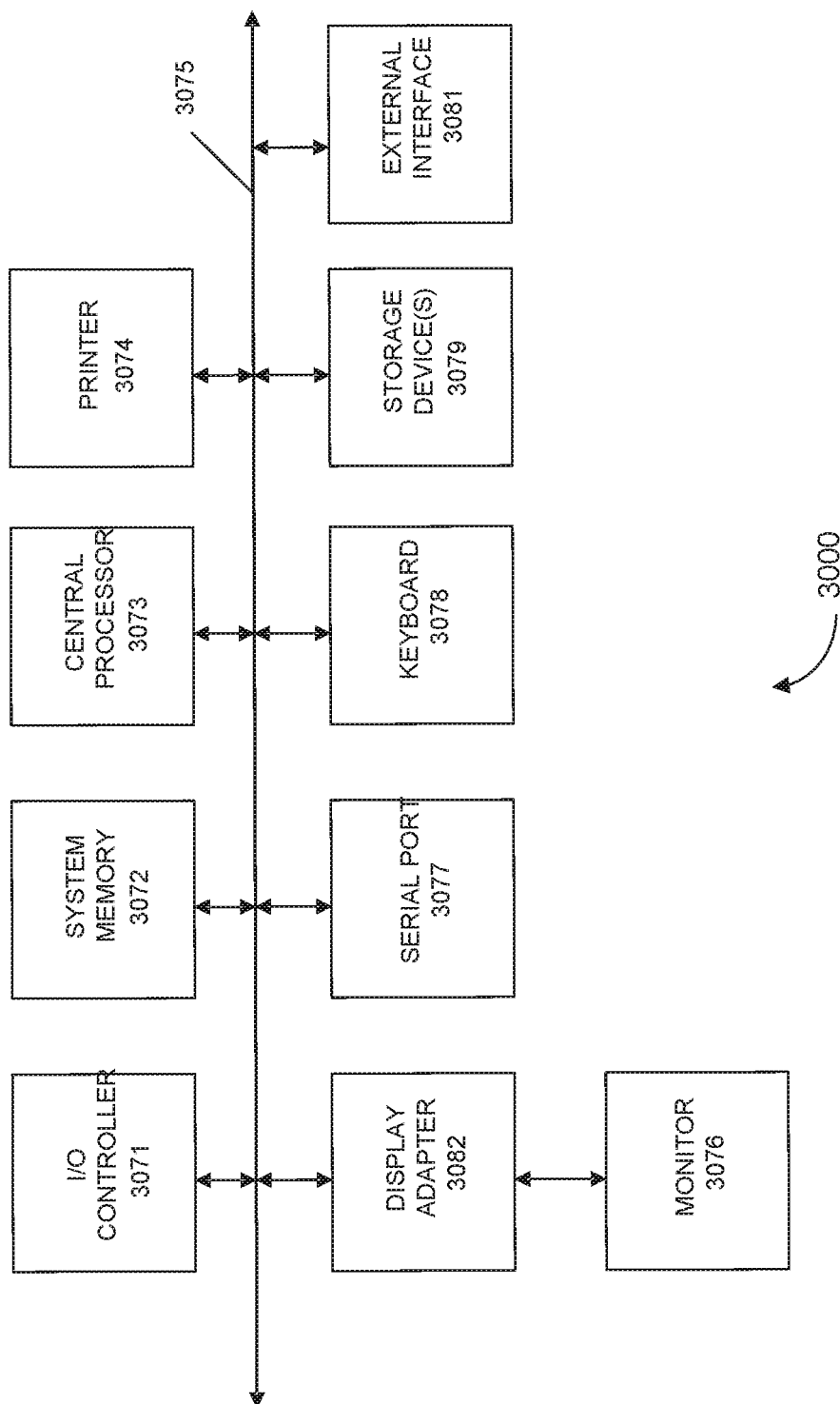


FIG. 30