|  |  |  |
| --- | --- | --- |
| **Mother Age (years)a** | 23.07±3.5 [18-33] | |
| **Mother Height (cms)a** | 152.33±5.9 [138.3-162.2] | |
| **POG (weeks)a** | 39.15±1.25 [37-41.6] | |
| **Infant Body weight (Kgs)a** | 2.8±0.35 [2.07-3.52] | |
| **Neonatal Sex** | **Female** | 26 (62%) |
| **Male** | 16 (38%) |
| **Parity** | **0** | 24 (57%) |
| **1** | 15 (36%) |
| **2** | 3 (7%) |
| **Maternal BMI group (at recruitment)** | **Normal Weight** | 24 (57%) |
| **Obese** | 2 (5%) |
| **Over weight** | 4 (9%) |
| **Under weight** | 12 (29%) |

**Table 1:** Participant information, a  Mean±Standard deviation [minimum-maximum].

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CpG ID** | **Gene Name** | **Region** | **Chr** | **Bonferroni adj. P** | **Pattern** | **11-14 weeks** | **18-20 weeks** | **26-28 weeks** | **At Delivery** |
| cg02561723 | CPA5 | Body | 7 | 2.29E-17 | P1(up-down-up) | 0.586 ± 0.017 | 0.616 ± 0.016 | 0.616 ± 0.014 | 0.659 ± 0.013 |
| cg09696231 | EPS15L1 | Body | 19 | 6.96E-10 | P1(up-down-up) | 0.396 ± 0.017 | 0.419 ± 0.014 | 0.419 ± 0.012 | 0.469 ± 0.012 |
| cg17521665 | PRDM1 | Body | 6 | 3.61E-10 | P1(up-down-up) | 0.522 ± 0.02 | 0.542 ± 0.017 | 0.541 ± 0.017 | 0.581 ± 0.018 |
| cg23079307 | SMAD7 | Body | 18 | 8.24E-11 | P1(up-down-up) | 0.55 ± 0.017 | 0.578 ± 0.015 | 0.57 ± 0.013 | 0.616 ± 0.013 |
| cg24761763 | EPHB1 | Body | 3 | 2.10E-10 | P1(up-down-up) | 0.606 ± 0.018 | 0.626 ± 0.015 | 0.623 ± 0.012 | 0.674 ± 0.012 |
| cg04987734 | CDC42BPB | Body | 14 | 3.81E-33 | P2(up-up-up) | 0.325 ± 0.013 | 0.349 ± 0.012 | 0.384 ± 0.012 | 0.426 ± 0.013 |
| cg07219384 | MAN1A1 | Body | 6 | 9.88E-21 | P2(up-up-up) | 0.344 ± 0.022 | 0.397 ± 0.022 | 0.408 ± 0.02 | 0.464 ± 0.019 |
| cg11132334 | TXK | TSS200 | 4 | 1.10E-23 | P2(up-up-up) | 0.316 ± 0.015 | 0.343 ± 0.013 | 0.368 ± 0.012 | 0.403 ± 0.011 |
| cg15791967 | KCNA3 | Body | 1 | 6.73E-22 | P2(up-up-up) | 0.405 ± 0.024 | 0.436 ± 0.022 | 0.457 ± 0.019 | 0.504 ± 0.018 |
| cg26277237 | KANK1 | 5'UTR | 9 | 2.09E-29 | P2(up-up-up) | 0.459 ± 0.02 | 0.512 ± 0.016 | 0.542 ± 0.015 | 0.597 ± 0.015 |
| cg05765440 | GNG12 | 5'UTR | 1 | 2.97E-06 | P3(up-up-down) | 0.609 ± 0.017 | 0.625 ± 0.02 | 0.659 ± 0.015 | 0.65 ± 0.015 |
| cg05869737 | APPBP2 | Body | 17 | 2.20E-06 | P3(up-up-down) | 0.543 ± 0.019 | 0.565 ± 0.022 | 0.574 ± 0.018 | 0.574 ± 0.019 |
| cg08459437 | CREB3L2 | Body | 7 | 4.02E-11 | P3(up-up-down) | 0.371 ± 0.016 | 0.409 ± 0.015 | 0.429 ± 0.016 | 0.429 ± 0.017 |
| cg15339796 | TRIB3 | Body | 20 | 5.75E-06 | P3(up-up-down) | 0.59 ± 0.021 | 0.618 ± 0.021 | 0.634 ± 0.019 | 0.632 ± 0.019 |
| cg19933954 | TCFL5 | TSS1500 | 20 | 4.61E-06 | P3(up-up-down) | 0.475 ± 0.023 | 0.498 ± 0.019 | 0.505 ± 0.018 | 0.449 ± 0.018 |
| cg06614199 | F13A1 | Body | 6 | 1.33E-08 | P4(down-up-up) | 0.36 ± 0.016 | 0.359 ± 0.017 | 0.389 ± 0.015 | 0.42 ± 0.013 |
| cg06994898 | SH3PXD2A | Body | 10 | 1.05E-05 | P4(down-up-up) | 0.399 ± 0.018 | 0.399 ± 0.014 | 0.409 ± 0.016 | 0.444 ± 0.018 |
| cg16754613 | ACSF3 | Body | 16 | 2.12E-06 | P4(down-up-up) | 0.449 ± 0.023 | 0.445 ± 0.025 | 0.462 ± 0.023 | 0.478 ± 0.021 |
| cg20744441 | VMP1 | Body | 17 | 5.76E-09 | P4(down-up-up) | 0.378 ± 0.015 | 0.376 ± 0.017 | 0.385 ± 0.014 | 0.419 ± 0.015 |
| cg25581222 | CSNK1G1 | Body | 15 | 2.46E-09 | P4(down-up-up) | 0.342 ± 0.015 | 0.341 ± 0.018 | 0.371 ± 0.021 | 0.393 ± 0.019 |
| cg00560428 | MAPK1 | Body | 22 | 3.88E-13 | P5(down-up-down) | 0.457 ± 0.019 | 0.427 ± 0.015 | 0.428 ± 0.015 | 0.397 ± 0.012 |
| cg05273620 | PRPF6 | Body | 20 | 1.67E-11 | P5(down-up-down) | 0.475 ± 0.023 | 0.45 ± 0.016 | 0.45 ± 0.016 | 0.4 ± 0.015 |
| cg10295552 | ACACA | Body | 17 | 3.49E-12 | P5(down-up-down) | 0.559 ± 0.02 | 0.538 ± 0.019 | 0.539 ± 0.018 | 0.494 ± 0.019 |
| cg13904258 | ARHGAP31 | Body | 3 | 3.32E-11 | P5(down-up-down) | 0.355 ± 0.016 | 0.338 ± 0.018 | 0.338 ± 0.016 | 0.315 ± 0.018 |
| cg19268453 | HLA-DMB | Body | 6 | 1.25E-12 | P5(down-up-down) | 0.377 ± 0.019 | 0.369 ± 0.019 | 0.37 ± 0.017 | 0.312 ± 0.014 |
| cg00868074 | ZCCHC14 | 3'UTR | 16 | 5.03E-28 | P6(down-down-down) | 0.638 ± 0.019 | 0.597 ± 0.019 | 0.58 ± 0.018 | 0.536 ± 0.016 |
| cg01826979 | NTRK3 | Body | 15 | 5.15E-31 | P6(down-down-down) | 0.588 ± 0.025 | 0.531 ± 0.022 | 0.483 ± 0.019 | 0.433 ± 0.018 |
| cg05186879 | MAPKAPK3 | 5'UTR | 3 | 2.26E-37 | P6(down-down-down) | 0.573 ± 0.013 | 0.541 ± 0.013 | 0.508 ± 0.015 | 0.482 ± 0.014 |
| cg07252680 | SERPINA1 | TSS200 | 14 | 6.43E-30 | P6(down-down-down) | 0.464 ± 0.015 | 0.423 ± 0.013 | 0.404 ± 0.01 | 0.343 ± 0.015 |
| cg12999836 | GRB10 | Body | 7 | 3.12E-29 | P6(down-down-down) | 0.629 ± 0.018 | 0.558 ± 0.013 | 0.538 ± 0.012 | 0.513 ± 0.013 |
| cg02133278 | TSKS | Body | 19 | 2.46E-05 | P7(down-down-up) | 0.656 ± 0.021 | 0.619 ± 0.019 | 0.619 ± 0.02 | 0.63 ± 0.022 |
| cg03585096 | PSPC1 | Body | 13 | 9.05E-04 | P7(down-down-up) | 0.474 ± 0.017 | 0.436 ± 0.016 | 0.432 ± 0.017 | 0.44 ± 0.017 |
| cg18942579 | TMEM49 | Body | 17 | 6.40E-04 | P7(down-down-up) | 0.433 ± 0.016 | 0.399 ± 0.017 | 0.385 ± 0.019 | 0.416 ± 0.018 |
| cg20090157 | LOC100996291 | TSS200 | 17 | 1.45E-13 | P7(down-down-up) | 0.591 ± 0.018 | 0.545 ± 0.017 | 0.532 ± 0.019 | 0.541 ± 0.02 |
| cg21489638 | LINC-PINT | Body | 7 | 5.47E-09 | P7(down-down-up) | 0.604 ± 0.016 | 0.589 ± 0.016 | 0.55 ± 0.013 | 0.557 ± 0.013 |
| cg00929635 | DBNDD2 | 5'UTR | 20 | 5.00E-12 | P8(up-down-down) | 0.403 ± 0.014 | 0.404 ± 0.014 | 0.383 ± 0.016 | 0.344 ± 0.017 |
| cg01542019 | TECR | Body | 19 | 5.46E-08 | P8(up-down-down) | 0.621 ± 0.017 | 0.623 ± 0.015 | 0.607 ± 0.016 | 0.585 ± 0.017 |
| cg10777461 | PEX14 | Body | 1 | 1.19E-07 | P8(up-down-down) | 0.5 ± 0.017 | 0.503 ± 0.019 | 0.478 ± 0.019 | 0.446 ± 0.016 |
| cg12234768 | LOC101928371 | Body | 2 | 8.61E-09 | P8(up-down-down) | 0.568 ± 0.027 | 0.576 ± 0.026 | 0.569 ± 0.022 | 0.516 ± 0.022 |
| cg21249371 | KDM2B | TSS200 | 12 | 9.85E-10 | P8(up-down-down) | 0.448 ± 0.021 | 0.45 ± 0.018 | 0.437 ± 0.018 | 0.403 ± 0.02 |

**Supplementary Table 1:** Summary statistics for 5 most significantly differentially methylated CpGs from each of the 8 temporal patterns. The beta values are provided as mean ± 95% confidence interval for each sampling timepoint.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ID** | **Description** | **Term P-Value Corrected with Bonferroni method** | **% Associated Genes** | **Number of Genes** | **Associated Genes Found** |
| GO:0043368 | positive T cell selection | 0.000001 | 32.50 | 13.00 | BATF, BCL11B, BCL2, DOCK2, IL12RB1, IL23A, ITPKB, LY9, PTPRC, SLAMF6, STAT3, THEMIS, TOX |
| GO:0045058 | T cell selection | 0.000001 | 28.30 | 15.00 | BATF, BCL11B, BCL2, CARD11, CD4, DOCK2, IL12RB1, IL23A, ITPKB, LY9, PTPRC, SLAMF6, STAT3, THEMIS, TOX |
| GO:0002715 | regulation of natural killer cell mediated immunity | 0.001022 | 22.00 | 11.00 | CD160, CD226, CD96, CRTAM, HLA-E, KLRK1, LILRB1, NCR1, RASGRP1, SLAMF6, STAT5B |
| GO:0042269 | regulation of natural killer cell mediated cytotoxicity | 0.002968 | 21.74 | 10.00 | CD160, CD226, CRTAM, HLA-E, KLRK1, LILRB1, NCR1, RASGRP1, SLAMF6, STAT5B |
| GO:0001912 | positive regulation of leukocyte mediated cytotoxicity | 0.006317 | 18.33 | 11.00 | CD160, CD226, CRTAM, HLA-E, IL12RB1, IL23A, KLRK1, PTPRC, RASGRP1, SLAMF6, STAT5B |
| GO:0050854 | regulation of antigen receptor-mediated signaling pathway | 0.003138 | 18.18 | 12.00 | CARD11, CD160, CD226, DUSP22, FCRL3, LAPTM5, LCK, PRKCH, PTPRC, PTPRJ, SLA2, UBASH3A |
| GO:0031343 | positive regulation of cell killing | 0.004288 | 17.65 | 12.00 | CD160, CD226, CRTAM, HLA-E, IL12RB1, IL23A, KLRK1, PRF1, PTPRC, RASGRP1, SLAMF6, STAT5B |
| GO:0046632 | alpha-beta T cell differentiation | 0.000007 | 17.36 | 21.00 | BATF, BCL11B, BCL2, CD86, IL12RB1, IL23A, IL4, IRF1, ITK, ITPKB, LEF1, LY9, PRDM1, RUNX1, SH3RF1, SLAMF6, SMAD7, STAT3, TGFBR2, TOX, ZC3H12A |
| GO:0046634 | regulation of alpha-beta T cell activation | 0.000022 | 16.95 | 20.00 | BATF, CARD11, CD160, CD86, CRTAM, HLA-E, IL12RB1, IL23A, IL4, IRF1, ITCH, ITPKB, LILRB1, PRDM1, PTPRC, RUNX1, SH3RF1, SMAD7, TGFBR2, ZC3H12A |
| GO:2000514 | regulation of CD4-positive, alpha-beta T cell activation | 0.005042 | 16.25 | 13.00 | BATF, CARD11, CD160, CD86, IL12RB1, IL23A, IL4, ITCH, RUNX1, SH3RF1, SMAD7, TGFBR2, ZC3H12A |
| GO:0032729 | positive regulation of interferon-gamma production | 0.005771 | 16.05 | 13.00 | CD160, CD226, CRTAM, IL12RB1, IL23A, ISL1, KLRK1, LILRB1, LTA, RASGRP1, SLAMF6, SLC11A1, TXK |
| GO:0046631 | alpha-beta T cell activation | 0.000000 | 15.93 | 29.00 | BATF, BCL11B, BCL2, CARD11, CD160, CD86, CRTAM, DOCK2, HLA-E, IL12RB1, IL23A, IL4, IRF1, ITCH, ITK, ITPKB, LEF1, LILRB1, LY9, PRDM1, PTPRC, RUNX1, SH3RF1, SLAMF6, SMAD7, STAT3, TGFBR2, TOX, ZC3H12A |
| GO:0097061 | dendritic spine organization | 0.003272 | 15.91 | 14.00 | ABI3, ARHGAP33, BAIAP2, CDK5, CTNND2, DOCK10, FYN, INSR, KALRN, LGMN, NLGN1, PPFIA2, SHANK1, STAU2 |
| GO:0001910 | regulation of leukocyte mediated cytotoxicity | 0.003730 | 15.73 | 14.00 | CD160, CD226, CRTAM, HLA-E, IL12RB1, IL23A, IL7R, KLRK1, LILRB1, NCR1, PTPRC, RASGRP1, SLAMF6, STAT5B |
| GO:0043367 | CD4-positive, alpha-beta T cell differentiation | 0.004243 | 15.56 | 14.00 | BATF, CD86, IL12RB1, IL23A, IL4, LEF1, LY9, RUNX1, SH3RF1, SLAMF6, SMAD7, STAT3, TOX, ZC3H12A |
| GO:0050852 | T cell receptor signaling pathway | 0.000018 | 15.33 | 23.00 | CARD11, CD160, CD226, CD8A, CD8B, CSK, CTLA4, DUSP22, FYN, ITK, LAPTM5, LCK, LCP2, LIME1, PIK3CD, PLCG1, PTPRC, PTPRJ, SLA2, THEMIS, TXK, UBASH3A, ZC3H12A |
| GO:0035710 | CD4-positive, alpha-beta T cell activation | 0.000436 | 15.25 | 18.00 | BATF, CARD11, CD160, CD86, IL12RB1, IL23A, IL4, ITCH, LEF1, LY9, RUNX1, SH3RF1, SLAMF6, SMAD7, STAT3, TGFBR2, TOX, ZC3H12A |
| GO:0033077 | T cell differentiation in thymus | 0.005460 | 15.22 | 14.00 | BCL11B, BCL2, CAMK4, CARD11, DOCK2, IL7R, ITPKB, PRKDC, PTPRC, RASGRP1, STAT5B, TNFRSF9, TOX, ZFP36L1 |
| GO:0031341 | regulation of cell killing | 0.002216 | 14.81 | 16.00 | CD160, CD226, CRTAM, HLA-E, IL12RB1, IL23A, IL4, IL7R, KLRK1, LILRB1, NCR1, PRF1, PTPRC, RASGRP1, SLAMF6, STAT5B |
| GO:0045580 | regulation of T cell differentiation | 0.000004 | 14.59 | 27.00 | ACTB, ARID1B, BATF, CAMK4, CARD11, CD86, CRTAM, CTLA4, IL12RB1, IL23A, IL4, IL7R, IRF1, ITPKB, LEF1, PRDM1, PTPRC, RASGRP1, RHOH, RUNX1, SH3RF1, SMAD7, SMARCA4, STAT5B, TGFBR2, TOX, ZC3H12A |
| GO:0045619 | regulation of lymphocyte differentiation | 0.000001 | 14.35 | 31.00 | ACTB, ARID1B, BATF, CAMK4, CARD11, CD86, CRTAM, CTLA4, FCRL3, IKZF3, IL12RB1, IL23A, IL4, IL7R, IRF1, ITPKB, LEF1, PRDM1, PRKDC, PTPRC, RASGRP1, RHOH, RUNX1, SH3RF1, SMAD7, SMARCA4, STAT5B, TGFBR2, TOX, ZC3H12A, ZFP36L1 |
| GO:0045639 | positive regulation of myeloid cell differentiation | 0.007003 | 14.15 | 15.00 | CD4, GPR68, HIF1A, IL23A, JAG1, LEF1, PPP3CA, PRKDC, ROR2, RUNX1, SMAP1, STAT1, STAT3, STAT5B, ZFP36L1 |
| GO:0030217 | T cell differentiation | 0.000000 | 14.01 | 44.00 | ACTB, ARID1B, BATF, BCL11B, BCL2, CAMK4, CARD11, CD4, CD86, CD8A, CRTAM, CTLA4, DOCK2, IKZF3, IL12RB1, IL23A, IL4, IL7R, IRF1, ITK, ITPKB, LCK, LEF1, LFNG, LY9, PIK3CD, PRDM1, PRKDC, PTPRC, RASGRP1, RHOH, RUNX1, SH3RF1, SLAMF6, SMAD7, SMARCA4, STAT3, STAT5B, TGFBR2, THEMIS, TNFRSF9, TOX, ZC3H12A, ZFP36L1 |
| GO:0045621 | positive regulation of lymphocyte differentiation | 0.002663 | 13.43 | 18.00 | ACTB, ARID1B, CD86, IL12RB1, IL23A, IL4, IL7R, ITPKB, LEF1, PRKDC, PTPRC, RASGRP1, RHOH, RUNX1, SMARCA4, STAT5B, TGFBR2, TOX |
| GO:0048813 | dendrite morphogenesis | 0.001048 | 13.33 | 20.00 | ABI3, ADGRB3, ARHGAP33, BAIAP2, CDK5, CTNND2, DCLK1, DOCK10, FBXO31, FYN, HECW1, HECW2, KALRN, NEDD4L, NLGN1, PPFIA2, PPP3CA, SEMA4D, SHANK1, STAU2 |
| GO:0045582 | positive regulation of T cell differentiation | 0.008334 | 13.33 | 16.00 | ACTB, ARID1B, CD86, IL12RB1, IL23A, IL4, IL7R, ITPKB, LEF1, PTPRC, RASGRP1, RHOH, RUNX1, SMARCA4, STAT5B, TGFBR2 |
| GO:1904019 | epithelial cell apoptotic process | 0.009394 | 12.69 | 17.00 | ADAR, BCL2, CD160, DAB2IP, ERC2, IL4, LEF1, PDCD4, PLCG1, RGCC, RYR2, STK24, STK3, TGFBR2, TNFAIP3, YAP1, ZFP36L1 |
| GO:0001909 | leukocyte mediated cytotoxicity | 0.007075 | 12.50 | 18.00 | CD160, CD226, CRTAM, CTSH, HLA-E, IL12RB1, IL23A, IL7R, KLRK1, LILRB1, NCR1, PRF1, PTPRC, RASGRP1, SLAMF6, SLAMF7, STAT5B, TTF2 |
| GO:0097553 | calcium ion transmembrane import into cytosol | 0.000558 | 12.31 | 24.00 | ADRA1A, BCL2, CACNA1A, CACNA1B, CACNA1E, CALM2, CASQ2, FYN, GRIN1, GSTO1, HTT, JPH1, LCK, LETM1, LIME1, NTSR1, PLCG1, PPP3CA, PTPRC, RYR2, TPCN2, TRDN, TRPM1, TTF2 |
| GO:1903708 | positive regulation of hemopoiesis | 0.001162 | 12.11 | 23.00 | ACTB, ARID1B, CD4, CD86, GPR68, IL12RB1, IL23A, IL4, IL7R, ITPKB, LEF1, PPP3CA, PRKDC, PTPRC, RASGRP1, RHOH, ROR2, RUNX1, SMARCA4, STAT5B, TGFBR2, TOX, ZFP36L1 |
| GO:1902107 | positive regulation of leukocyte differentiation | 0.001162 | 12.11 | 23.00 | ACTB, ARID1B, CD4, CD86, GPR68, IL12RB1, IL23A, IL4, IL7R, ITPKB, LEF1, PPP3CA, PRKDC, PTPRC, RASGRP1, RHOH, ROR2, RUNX1, SMARCA4, STAT5B, TGFBR2, TOX, ZFP36L1 |
| GO:0030098 | lymphocyte differentiation | 0.000000 | 12.10 | 53.00 | ACTB, ARID1B, BATF, BCL11B, BCL2, CAMK4, CARD11, CD4, CD79A, CD86, CD8A, CRTAM, CTLA4, DOCK10, DOCK2, FCRL3, IKZF1, IKZF3, IL12RB1, IL23A, IL4, IL7R, IRF1, ITK, ITPKB, KLF6, LCK, LEF1, LFNG, LRRC8A, LY9, PAX5, PIK3CD, PRDM1, PRKDC, PTPRC, PTPRJ, RASGRP1, RHOH, RUNX1, SH3RF1, SLAMF6, SMAD7, SMARCA4, ST3GAL1, STAT3, STAT5B, TGFBR2, THEMIS, TNFRSF9, TOX, ZC3H12A, ZFP36L1 |
| GO:0050863 | regulation of T cell activation | 0.000000 | 11.93 | 47.00 | ACTB, ARID1B, BATF, CAMK4, CARD11, CD160, CD4, CD5, CD6, CD86, CRTAM, CSK, CTLA4, DUSP22, FYN, HLA-E, IL12RB1, IL23A, IL4, IL6ST, IL7R, IRF1, ITCH, ITPKB, KLRK1, LAPTM5, LAT, LAX1, LCK, LEF1, LILRB1, NCK1, PPP3CA, PRDM1, PTPRC, RASGRP1, RHOH, RUNX1, SH3RF1, SLC7A1, SMAD7, SMARCA4, STAT5B, TGFBR2, TNFRSF9, TOX, ZC3H12A |
| GO:0050870 | positive regulation of T cell activation | 0.000047 | 11.92 | 31.00 | ACTB, ARID1B, CARD11, CD160, CD4, CD5, CD6, CD86, CSK, FYN, HLA-E, IL12RB1, IL23A, IL4, IL6ST, IL7R, ITPKB, KLRK1, LCK, LEF1, LILRB1, NCK1, PPP3CA, PTPRC, RASGRP1, RHOH, RUNX1, SLC7A1, SMARCA4, STAT5B, TGFBR2 |
| GO:1902105 | regulation of leukocyte differentiation | 0.000005 | 11.59 | 38.00 | ACTB, ARID1B, BATF, CAMK4, CARD11, CD4, CD86, CRTAM, CTLA4, FCRL3, GPR68, IKZF3, IL12RB1, IL23A, IL4, IL7R, IRF1, ITPKB, LEF1, LILRB1, MITF, PPP3CA, PRDM1, PRKDC, PTPRC, RASGRP1, RBP1, RHOH, ROR2, RUNX1, SH3RF1, SMAD7, SMARCA4, STAT5B, TGFBR2, TOX, ZC3H12A, ZFP36L1 |
| GO:1903131 | mononuclear cell differentiation | 0.000000 | 11.41 | 56.00 | ACTB, ARID1B, BATF, BCL11B, BCL2, CAMK4, CARD11, CD4, CD79A, CD86, CD8A, CRTAM, CTLA4, DOCK10, DOCK2, FCRL3, GPR68, IKZF1, IKZF3, IL12RB1, IL23A, IL4, IL7R, IRF1, ITK, ITPKB, KLF6, LCK, LEF1, LFNG, LILRB1, LRRC8A, LY9, MYH9, PAX5, PIK3CD, PRDM1, PRKDC, PTPRC, PTPRJ, RASGRP1, RHOH, RUNX1, SH3RF1, SLAMF6, SMAD7, SMARCA4, ST3GAL1, STAT3, STAT5B, TGFBR2, THEMIS, TNFRSF9, TOX, ZC3H12A, ZFP36L1 |
| GO:0042110 | T cell activation | 0.000000 | 11.38 | 66.00 | ACTB, ARID1B, BATF, BCL11B, BCL2, CAMK4, CARD11, CD160, CD4, CD5, CD6, CD86, CD8A, CD8B, CRTAM, CSK, CTLA4, DOCK2, DUSP22, FYN, HLA-E, IKZF3, IL12RB1, IL23A, IL4, IL6ST, IL7R, IRF1, ITCH, ITK, ITPKB, KLRK1, LAPTM5, LAT, LAX1, LCK, LEF1, LFNG, LILRB1, LY9, MYH9, NCK1, PIK3CD, PPP3CA, PRDM1, PRKDC, PTPRC, RASGRP1, RHOH, RUNX1, SH3RF1, SLA2, SLAMF6, SLAMF7, SLC11A1, SLC7A1, SMAD7, SMARCA4, STAT3, STAT5B, TGFBR2, THEMIS, TNFRSF9, TOX, ZC3H12A, ZFP36L1 |
| GO:0042098 | T cell proliferation | 0.002343 | 11.06 | 25.00 | CARD11, CD6, CD86, CRTAM, CTLA4, DOCK2, FYN, HLA-E, IL12RB1, IL23A, IL4, IL6ST, IRF1, ITCH, LILRB1, NCK1, PPP3CA, PTPRC, RASGRP1, SH3RF1, SLC11A1, SLC7A1, STAT5B, TGFBR2, TNFRSF9 |
| GO:1903039 | positive regulation of leukocyte cell-cell adhesion | 0.000315 | 10.92 | 31.00 | ACTB, ARID1B, CARD11, CD160, CD4, CD5, CD6, CD86, CSK, FYN, HLA-E, IL12RB1, IL23A, IL4, IL6ST, IL7R, ITPKB, KLRK1, LCK, LEF1, LILRB1, NCK1, PPP3CA, PTPRC, RASGRP1, RHOH, RUNX1, SLC7A1, SMARCA4, STAT5B, TGFBR2 |
| GO:0045637 | regulation of myeloid cell differentiation | 0.005001 | 10.81 | 24.00 | CAMK4, CD4, GPR171, GPR68, HIF1A, IL23A, IL4, ITPKB, JAG1, LEF1, LILRB1, MEF2C, MITF, PEX2, PPP3CA, PRKDC, RBP1, ROR2, RUNX1, SMAP1, STAT1, STAT3, STAT5B, ZFP36L1 |
| GO:0022409 | positive regulation of cell-cell adhesion | 0.000066 | 10.78 | 36.00 | ACTB, ARID1B, CARD11, CD160, CD4, CD5, CD6, CD86, CSK, EMILIN2, FLOT1, FYN, HLA-E, IL12RB1, IL23A, IL4, IL6ST, IL7R, ITPKB, KIF26B, KLRK1, LCK, LEF1, LILRB1, MYO10, NCK1, PPP3CA, PTPRC, RASGRP1, RHOH, RUNX1, SLC7A1, SMAD7, SMARCA4, STAT5B, TGFBR2 |
| GO:0032944 | regulation of mononuclear cell proliferation | 0.001243 | 10.77 | 28.00 | BCL2, CARD11, CD6, CD86, CRTAM, CTLA4, FCRL3, HLA-E, IKZF3, IL12RB1, IL23A, IL4, IL6ST, IRF1, ITCH, LILRB1, MEF2C, NCK1, PPP3CA, PTPRC, RASSF5, SH3RF1, SLC7A1, SLCO1B1, ST6GAL1, STAT5B, TGFBR2, TNFRSF9 |
| GO:1903706 | regulation of hemopoiesis | 0.000002 | 10.75 | 46.00 | ACTB, ARID1B, BATF, CAMK4, CARD11, CD4, CD86, CRTAM, CTLA4, FCRL3, GPR171, GPR68, HIF1A, IKZF3, IL12RB1, IL23A, IL4, IL7R, IRF1, ITPKB, JAG1, LEF1, LILRB1, MEF2C, MITF, PEX2, PPP3CA, PRDM1, PRKDC, PTPRC, RASGRP1, RBP1, RHOH, ROR2, RUNX1, SH3RF1, SMAD7, SMAP1, SMARCA4, STAT1, STAT3, STAT5B, TGFBR2, TOX, ZC3H12A, ZFP36L1 |
| GO:0016358 | dendrite development | 0.001337 | 10.73 | 28.00 | ABI3, ADGRB3, ARHGAP33, BAIAP2, CAMK1D, CDK5, CTNND2, DAB2IP, DCLK1, DISC1, DOCK10, FAT3, FBXO31, FYN, HECW1, HECW2, IQSEC1, KALRN, LAMC2, MEF2C, NEDD4L, NLGN1, PPFIA2, PPP3CA, SEMA4D, SHANK1, SLCO1B1, STAU2 |
| GO:0015276 | ligand-gated ion channel activity | 0.004232 | 10.68 | 25.00 | ABCC8, ANXA6, CALM2, CASQ2, CFTR, CHRNA1, CHRNB1, CHRNB3, GABRG3, GRIN1, GSG1L, GSTO1, HCN2, HCN4, HTR3B, HTT, JPH1, MEF2C, NLGN1, OPRM1, RASGRF2, RYR2, SHANK1, TPCN2, TRDN |
| GO:0022834 | ligand-gated channel activity | 0.004232 | 10.68 | 25.00 | ABCC8, ANXA6, CALM2, CASQ2, CFTR, CHRNA1, CHRNB1, CHRNB3, GABRG3, GRIN1, GSG1L, GSTO1, HCN2, HCN4, HTR3B, HTT, JPH1, MEF2C, NLGN1, OPRM1, RASGRF2, RYR2, SHANK1, TPCN2, TRDN |
| GO:0050851 | antigen receptor-mediated signaling pathway | 0.001228 | 10.64 | 30.00 | BCL2, CARD11, CD160, CD226, CD79A, CD8A, CD8B, CSK, CTLA4, DUSP22, FCRL3, FYN, ITK, LAPTM5, LAX1, LCK, LCP2, LIME1, MEF2C, PIK3CD, PLCG1, PRKCH, PTPRC, PTPRJ, SH2B2, SLA2, THEMIS, TXK, UBASH3A, ZC3H12A |
| GO:0050670 | regulation of lymphocyte proliferation | 0.002265 | 10.63 | 27.00 | BCL2, CARD11, CD6, CD86, CRTAM, CTLA4, FCRL3, HLA-E, IKZF3, IL12RB1, IL23A, IL4, IL6ST, IRF1, ITCH, LILRB1, MEF2C, NCK1, PPP3CA, PTPRC, RASSF5, SH3RF1, SLC7A1, SLCO1B1, STAT5B, TGFBR2, TNFRSF9 |
| GO:0046651 | lymphocyte proliferation | 0.000296 | 10.56 | 34.00 | BCL2, CARD11, CD6, CD79A, CD86, CRTAM, CTLA4, DOCK2, FCRL3, FYN, HLA-E, IKZF3, IL12RB1, IL23A, IL4, IL6ST, IL7R, IRF1, ITCH, LEF1, LILRB1, MEF2C, NCK1, PPP3CA, PTPRC, RASGRP1, RASSF5, SH3RF1, SLC11A1, SLC7A1, SLCO1B1, STAT5B, TGFBR2, TNFRSF9 |
| GO:0032943 | mononuclear cell proliferation | 0.000209 | 10.54 | 35.00 | BCL2, CARD11, CD6, CD79A, CD86, CRTAM, CTLA4, DOCK2, FCRL3, FYN, HLA-E, IKZF3, IL12RB1, IL23A, IL4, IL6ST, IL7R, IRF1, ITCH, LEF1, LILRB1, MEF2C, NCK1, PPP3CA, PTPRC, RASGRP1, RASSF5, SH3RF1, SLC11A1, SLC7A1, SLCO1B1, ST6GAL1, STAT5B, TGFBR2, TNFRSF9 |
| GO:0007159 | leukocyte cell-cell adhesion | 0.000009 | 10.50 | 44.00 | ACTB, ARID1B, CARD11, CD160, CD4, CD5, CD6, CD86, CRTAM, CSK, CTLA4, DUSP22, FYN, HLA-E, IL12RB1, IL23A, IL4, IL6ST, IL7R, IRF1, ITCH, ITPKB, KLRK1, LAPTM5, LAX1, LCK, LEF1, LILRB1, NCK1, PODXL2, PPP3CA, PTPRC, RASGRP1, RHOH, ROCK1, RUNX1, SEMA4D, SLC7A1, SMAD7, SMARCA4, STAT5B, STK10, TGFBR2, ZC3H12A |
| GO:1903037 | regulation of leukocyte cell-cell adhesion | 0.000036 | 10.50 | 40.00 | ACTB, ARID1B, CARD11, CD160, CD4, CD5, CD6, CD86, CRTAM, CSK, CTLA4, DUSP22, FYN, HLA-E, IL12RB1, IL23A, IL4, IL6ST, IL7R, IRF1, ITCH, ITPKB, KLRK1, LAPTM5, LAX1, LCK, LEF1, LILRB1, NCK1, PPP3CA, PTPRC, RASGRP1, RHOH, RUNX1, SLC7A1, SMAD7, SMARCA4, STAT5B, TGFBR2, ZC3H12A |
| GO:0070663 | regulation of leukocyte proliferation | 0.001402 | 10.49 | 30.00 | BCL2, CARD11, CD6, CD86, CRTAM, CTLA4, FCRL3, HLA-E, IKZF3, IL12RB1, IL23A, IL4, IL6ST, IRF1, ITCH, LILRB1, MEF2C, NCK1, PPP3CA, PTK2, PTPRC, RASSF5, SH3RF1, SLC7A1, SLCO1B1, ST6GAL1, STAT5B, TGFBR2, TNFAIP3, TNFRSF9 |
| GO:0022898 | regulation of transmembrane transporter activity | 0.001031 | 10.44 | 31.00 | ABCC8, ACTB, BCL2, CACNA1A, CALM2, CASQ2, CDK5, CFTR, GSG1L, GSTO1, HCN2, HCN4, HECW1, HECW2, HTT, JPH1, MEF2C, NEDD4L, NLGN1, NTSR1, OPRM1, PPP3CA, RASGRF2, RYR2, SHANK1, SLMAP, STIM2, TRDN, UTRN, VMP1, YWHAE |
| GO:0032412 | regulation of ion transmembrane transporter activity | 0.002968 | 10.18 | 29.00 | ABCC8, CACNA1A, CALM2, CASQ2, CDK5, CFTR, GSG1L, GSTO1, HCN2, HCN4, HECW1, HECW2, HTT, JPH1, MEF2C, NEDD4L, NLGN1, NTSR1, OPRM1, PPP3CA, RASGRF2, RYR2, SHANK1, SLMAP, STIM2, TRDN, UTRN, VMP1, YWHAE |

**Supplementary Table 2:** Significantly enriched GO-Biological Processes enriched using the progressively hypermethylated (Up trending) genes during the period of gestation.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Celltype** | **Reference** | **Compare group** | **P-value** | **Benjamini-Hochberg adjusted P-value** |
| Granulocytes | V1 | V4 | 0.00000000173 | 0.00000000519 |
| CD8T | V1 | V4 | 0.00000000559 | 0.0000000168 |
| CD4T | V1 | V4 | 0.0000000924 | 0.000000277 |
| Bcell | V1 | V4 | 0.000000458 | 0.00000137 |
| NK | V1 | V4 | 0.000175 | 0.000525 |
| Monocytes | V1 | V4 | 0.001 | 0.004 |
| Granulocytes | V1 | V3 | 0.003 | 0.006 |
| Bcell | V1 | V3 | 0.006 | 0.013 |
| CD4T | V1 | V3 | 0.006 | 0.013 |
| Granulocytes | V1 | V2 | 0.036 | 0.036 |
| Bcell | V1 | V2 | 0.04 | 0.04 |
| NK | V1 | V3 | 0.027 | 0.055 |
| Monocytes | V1 | V3 | 0.041 | 0.083 |
| CD8T | V1 | V3 | 0.046 | 0.093 |
| CD4T | V1 | V2 | 0.094 | 0.094 |
| CD8T | V1 | V2 | 0.209 | 0.209 |
| NK | V1 | V2 | 0.213 | 0.213 |
| Monocytes | V1 | V2 | 0.295 | 0.295 |

**Supplementary Table 3:** List of celltype proportions that changes during pregnancy (compared to the 1st timepoint) and their corresponding p-values.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ID** | **Description** | **Term P-Value Corrected with Bonferroni method** | **% Associated Genes** | **Number of Genes** | **Associated Genes Found** |
| GO:0034204 | lipid translocation | 0.01 | 22.95 | 14.00 | ABCA1, ABCC1, ABCG1, ANO6, ANO7, ATP10A, ATP11A, ATP11B, ATP8B2, ATP8B4, ATP9A, KCNN4, MFSD2A, P2RX7 |
| GO:0090630 | activation of GTPase activity | 0.00 | 18.25 | 23.00 | ABR, AGAP2, AGAP7P, ARHGAP22, ARHGEF26, BCR, CORO1C, EPHA1, NDEL1, NTRK3, RABGAP1, RALGAPA2, RALGAPB, RAP1GAP, RCC2, SCRIB, SIPA1, SIPA1L1, SIPA1L3, TBC1D1, TBC1D14, TBC1D22B, TBC1D8 |
| GO:0001952 | regulation of cell-matrix adhesion | 0.00 | 17.42 | 23.00 | ABL1, CDK6, CLASP1, CORO1C, DAG1, DLC1, EFNA5, ENC1, EPHA1, FMN1, ITGB1BP1, JUP, LIMS1, MACF1, NF1, NRP1, PIK3R1, PRKCZ, RCC2, RIN2, SMAD3, SRC, SYNGAP1 |
| GO:0005096 | GTPase activator activity | 0.00 | 16.44 | 48.00 | ABR, ACAP1, AGAP2, AGAP7P, ANKRD27, ARAP1, ARAP2, ARHGAP15, ARHGAP17, ARHGAP21, ARHGAP22, ARHGAP26, ARHGAP27, ARHGAP31, ARHGEF10L, BCR, CHN1, DLC1, DOCK1, DOCK4, GNB5, IQGAP2, NF1, NPRL3, NRP1, PREX1, RABGAP1, RALGAPA2, RALGAPB, RAP1GAP, RASA3, RGS3, RGS6, RGS9, RIN2, RINL, SIPA1, SIPA1L1, SIPA1L3, STARD13, SYNGAP1, TBC1D1, TBC1D14, TBC1D22B, TBC1D8, TBCD, UNC45A, VAV3 |
| GO:0010810 | regulation of cell-substrate adhesion | 0.00 | 15.09 | 35.00 | ABL1, ACTN4, ANGPT2, CDK6, CLASP1, CORO1C, DAG1, DLC1, DOCK1, EFNA5, EMILIN1, ENC1, EPHA1, FMN1, GCNT2, ITGA5, ITGB1BP1, JUP, LIMS1, MACF1, NDNF, NF1, NOTCH1, NRP1, PIK3R1, PREX1, PRKCE, PRKCZ, RCC2, RIN2, RREB1, SMAD3, SRC, SYNGAP1, TBCD |
| GO:0051495 | positive regulation of cytoskeleton organization | 0.01 | 14.78 | 30.00 | ABI2, ABL1, ANKRD53, ARHGEF10L, BIN1, BMP10, CDC42EP3, CLASP1, CSF3, DRG1, DYNC1H1, EPHA1, FMN1, GRB2, ITGB1BP1, MET, NAV3, NDRG1, NRP1, NTRK3, NUMA1, P2RX7, PRKCE, PXDN, PXN, SMAD3, STAP1, TRIM27, VTA1, WASL |
| GO:0043087 | regulation of GTPase activity | 0.00 | 14.43 | 57.00 | ABR, AGAP2, AGAP7P, ARAP1, ARAP2, ARHGAP15, ARHGAP22, ARHGAP27, ARHGEF26, BCR, BIN1, CCL22, CCPG1, CHN1, CORO1C, DENND1A, EFNA5, EIF2S1, EPHA1, FGD4, GNB5, IQGAP2, ITGA6, ITGB1BP1, LIMS1, LRCH1, MET, MRAP, NDEL1, NF1, NTRK3, PDZD2, PKP4, PREX1, RABGAP1, RALGAPA2, RALGAPB, RAP1GAP, RAPGEF4, RASA3, RASGEF1A, RCC2, RDX, RGS6, RGS9, SCRIB, SIPA1, SIPA1L1, SIPA1L3, SYNGAP1, TBC1D1, TBC1D14, TBC1D22B, TBC1D8, TRAPPC6A, VAV3, WNK1 |
| GO:0007160 | cell-matrix adhesion | 0.00 | 14.40 | 36.00 | ABL1, BCR, CDK6, CLASP1, CORO1C, DAG1, DLC1, EFNA5, EMILIN1, ENC1, EPHA1, FMN1, ITGA2B, ITGA5, ITGA6, ITGAE, ITGAL, ITGB1BP1, JUP, LIMS1, MACF1, MKLN1, NF1, NRP1, PIK3R1, PPFIA1, PRKCZ, PXDN, PXN, RCC2, RIN2, SMAD3, SNED1, SRC, SYNGAP1, TNN |
| GO:0060589 | nucleoside-triphosphatase regulator activity | 0.00 | 14.31 | 76.00 | ABR, ACAP1, AGAP2, AGAP7P, AKAP13, ANKRD27, ARAP1, ARAP2, ARHGAP15, ARHGAP17, ARHGAP21, ARHGAP22, ARHGAP26, ARHGAP27, ARHGAP31, ARHGEF10L, ARHGEF26, ARHGEF28, BCR, CCPG1, CHN1, DENND1A, DENND3, DENND4A, DLC1, DOCK1, DOCK4, EIF2S1, ETFDH, FARP2, FGD4, FNIP1, GNB5, GPS1, IPO7, IQGAP2, ITGB1BP1, ITSN2, LAMTOR3, MCF2L2, MET, MRAP, NF1, NPRL3, NRP1, PISD, PLCE1, PREX1, RABGAP1, RABGEF1, RALGAPA2, RALGAPB, RAP1GAP, RAPGEF4, RASA3, RASGEF1A, RCC2, RGS3, RGS6, RGS9, RIN2, RINL, SIPA1, SIPA1L1, SIPA1L3, STARD13, SYNGAP1, TBC1D1, TBC1D14, TBC1D22B, TBC1D8, TBCD, TNK2, UNC45A, VAV3, WASL |
| GO:0030695 | GTPase regulator activity | 0.00 | 14.31 | 76.00 | ABR, ACAP1, AGAP2, AGAP7P, AKAP13, ANKRD27, ARAP1, ARAP2, ARHGAP15, ARHGAP17, ARHGAP21, ARHGAP22, ARHGAP26, ARHGAP27, ARHGAP31, ARHGEF10L, ARHGEF26, ARHGEF28, BCR, CCPG1, CHN1, DENND1A, DENND3, DENND4A, DLC1, DOCK1, DOCK4, EIF2S1, ETFDH, FARP2, FGD4, FNIP1, GNB5, GPS1, IPO7, IQGAP2, ITGB1BP1, ITSN2, LAMTOR3, MCF2L2, MET, MRAP, NF1, NPRL3, NRP1, PISD, PLCE1, PREX1, RABGAP1, RABGEF1, RALGAPA2, RALGAPB, RAP1GAP, RAPGEF4, RASA3, RASGEF1A, RCC2, RGS3, RGS6, RGS9, RIN2, RINL, SIPA1, SIPA1L1, SIPA1L3, STARD13, SYNGAP1, TBC1D1, TBC1D14, TBC1D22B, TBC1D8, TBCD, TNK2, UNC45A, VAV3, WASL |
| GO:0051056 | regulation of small GTPase mediated signal transduction | 0.00 | 14.12 | 48.00 | ABCA1, ABL1, ABR, AKAP13, ARAP1, ARHGAP15, ARHGAP17, ARHGAP21, ARHGAP22, ARHGAP26, ARHGAP27, ARHGAP31, ARHGEF10L, ARHGEF28, BCR, CHN1, DENND1A, DENND3, DENND4A, DLC1, ETFDH, FGD4, HEG1, MAPKAP1, MET, MRAP, NF1, NOTCH1, NRP1, PISD, PLCE1, PREX1, RABGEF1, RALGAPA2, RALGAPB, RAP1GAP, RASA3, RASGEF1A, RDX, SCAI, SIPA1, SIPA1L1, SIPA1L3, SQSTM1, SRC, STARD13, SYNGAP1, VAV3 |
| GO:0043547 | positive regulation of GTPase activity | 0.00 | 13.86 | 42.00 | ABR, AGAP2, AGAP7P, ARAP1, ARAP2, ARHGAP22, ARHGAP27, ARHGEF26, BCR, BIN1, CCL22, CHN1, CORO1C, DENND1A, EPHA1, GNB5, ITGA6, LIMS1, NDEL1, NF1, NTRK3, PDZD2, PKP4, PREX1, RABGAP1, RALGAPA2, RALGAPB, RAP1GAP, RAPGEF4, RASGEF1A, RCC2, RGS6, RGS9, SCRIB, SIPA1, SIPA1L1, SIPA1L3, SYNGAP1, TBC1D1, TBC1D14, TBC1D22B, TBC1D8 |
| GO:0030336 | negative regulation of cell migration | 0.01 | 12.99 | 40.00 | AKT1, ALOX15B, ANGPT2, ATP2B4, BCR, BMP10, BST2, CLASP1, CORO1C, CYP19A1, DAG1, DLC1, DLG5, EMILIN1, ENC1, ENG, EPHA1, GNA12, IGFBP5, ITGB1BP1, JUP, LRCH1, MCC, NAV3, NBL1, NF1, NFE2L2, NISCH, NOTCH1, RABGEF1, S100A8, SCAI, SERPINF1, STAP1, STARD13, TMIGD3, TNN, VASH1, WASL, ZMYND8 |
| GO:0031589 | cell-substrate adhesion | 0.00 | 12.92 | 50.00 | ABL1, ACTN4, ANGPT2, ANTXR1, BCR, CDK6, CLASP1, CORO1C, DAG1, DLC1, DOCK1, EFNA5, EMILIN1, ENC1, EPHA1, FMN1, GCNT2, ITGA2B, ITGA5, ITGA6, ITGAE, ITGAL, ITGB1BP1, JUP, LIMS1, MACF1, MERTK, MKLN1, MYO1G, NDNF, NF1, NOTCH1, NRP1, PIK3R1, PPFIA1, PREX1, PRKCE, PRKCZ, PXDN, PXN, RADIL, RCC2, RIN2, RREB1, SMAD3, SNED1, SRC, SYNGAP1, TBCD, TNN |
| GO:0040013 | negative regulation of locomotion | 0.00 | 12.71 | 46.00 | AKT1, ALOX15B, ANGPT2, ATP2B4, BCR, BMP10, BST2, CLASP1, CORO1C, CYP19A1, DAG1, DLC1, DLG5, EMILIN1, ENC1, ENG, EPHA1, GNA12, IGFBP5, ITGB1BP1, JUP, LRCH1, MCC, NAV3, NBL1, NF1, NFE2L2, NISCH, NOTCH1, NRP1, PDZD2, RABGEF1, S100A8, SCAI, SEMA3C, SEMA4B, SEMA6B, SERPINF1, SLIT1, STAP1, STARD13, TMIGD3, TNN, VASH1, WASL, ZMYND8 |
| GO:0008047 | enzyme activator activity | 0.00 | 11.42 | 69.00 | ABR, ACAP1, AGAP2, AGAP7P, ALOX5AP, ANKRD27, ARAP1, ARAP2, ARHGAP15, ARHGAP17, ARHGAP21, ARHGAP22, ARHGAP26, ARHGAP27, ARHGAP31, ARHGEF10L, ATP2A3, AZIN2, BCR, BMPR1B, CAB39, CHN1, DAXX, DLC1, DOCK1, DOCK4, EFNA5, ETFDH, GNB5, IQGAP2, LAMTOR3, MAL, NF1, NPRL3, NRP1, PCOLCE2, PHACTR4, PPP4R3B, PREX1, PRKCE, RABGAP1, RALGAPA2, RALGAPB, RAP1GAP, RASA3, RGS3, RGS6, RGS9, RIN2, RINL, SIPA1, SIPA1L1, SIPA1L3, SLC19A1, SLX4, SRC, STAP1, STARD13, SYNGAP1, TAB1, TAOK1, TBC1D1, TBC1D14, TBC1D22B, TBC1D8, TBCD, UNC45A, VAV3, WNK1 |
| GO:0007264 | small GTPase mediated signal transduction | 0.00 | 11.35 | 63.00 | ABCA1, ABI2, ABL1, ABR, AKAP13, ARAP1, ARHGAP15, ARHGAP17, ARHGAP21, ARHGAP22, ARHGAP26, ARHGAP27, ARHGAP31, ARHGEF10L, ARHGEF28, BCR, CDC42EP3, CHN1, DENND1A, DENND3, DENND4A, DLC1, DOCK1, DOCK4, ETFDH, FARP2, FGD4, GNA12, GRB2, HEG1, MAPKAP1, MET, MRAP, NF1, NISCH, NOTCH1, NRP1, PHACTR4, PISD, PLCE1, PREX1, RABGEF1, RALGAPA2, RALGAPB, RAP1GAP, RAPGEF4, RASA3, RASGEF1A, RDX, RHOBTB3, RIN2, SCAI, SETDB1, SHTN1, SIPA1, SIPA1L1, SIPA1L3, SQSTM1, SRC, STARD13, SYNGAP1, TNK2, VAV3 |
| GO:1902532 | negative regulation of intracellular signal transduction | 0.00 | 11.33 | 62.00 | ABL1, ADGRG3, AKT1, ATP2B4, BANK1, BCL2L1, C1QTNF3, C3orf33, CLU, DAG1, DLC1, DLG5, DYRK1A, EMILIN1, ENO1, ESR1, FNIP1, FOXO1, GBAP1, HEG1, ITGB1BP1, MAPK14, MAPK7, MAPKAP1, MECOM, MET, MGRN1, MYC, MYO1C, NF1, NFE2L2, NLRP3, NOL3, NPRL3, OPRL1, P2RX7, PDE11A, PDZD2, PPM1A, PRDM15, PTPN1, RABGEF1, RASA3, RCAN1, RRM2B, S100A8, SCAI, SEC14L1, SESN1, SH3RF2, SORL1, SPRED2, SRC, SYNGAP1, TLE1, TRIM39, TRIM40, USP10, USP47, VGLL4, WNK2, ZMYND11 |
| GO:0030036 | actin cytoskeleton organization | 0.00 | 11.25 | 87.00 | ABI2, ABL1, ACTN4, ADD1, AGAP2, AKAP13, ALMS1, ANTXR1, ARAP1, ARHGAP17, ARHGAP26, ARHGEF10L, BCR, BIN1, BMP10, BST2, CDC42EP3, CLASP1, CLU, CORO1C, CSF3, CXADR, DAAM1, DAAM2, DIAPH3, DLC1, DNAJB6, DTNBP1, EFNA5, EPHA1, FARP2, FGD4, FHL3, FMN1, GAS7, GRB2, IQGAP2, ITGB1BP1, LIMA1, MARCKS, MET, MKLN1, MRAP, MYO1B, MYO1C, MYO1E, MYO1F, MYO1G, MYOM2, NF1, NISCH, NPHP4, NRP1, NTRK3, PACSIN2, PAWR, PDLIM7, PHACTR3, PHACTR4, PIK3R1, PIP5K1C, PPFIA1, PREX1, PRKCE, PSTPIP2, PTPN1, PXDN, PXN, RDX, RHOBTB3, RUFY3, SHTN1, SIPA1L1, SMAD3, SPECC1, SPIRE1, SRC, SSH1, STAP1, STARD13, SYNGAP1, TAOK1, TPM2, TPM3, TRIM27, TRPM2, WASL |
| GO:0003013 | circulatory system process | 0.00 | 11.15 | 71.00 | ABCC1, ABCG2, ABL1, AKAP13, ANK2, ATP2A3, ATP2B4, AZU1, BCR, BIN1, BMP10, C3AR1, CACNA1C, CELF2, CHD7, CHRM3, CTNNBIP1, CTSZ, CXADR, DOCK4, ECE1, EMILIN1, ERAP1, EXT1, FABP5, FFAR3, FLI1, FXYD1, GJA5, GNA11, GNA12, HDAC4, HEG1, HOPX, ITGB1BP1, JUP, KCNE1, KCNQ1, KCTD11, LEP, LRP2, MFSD2A, NANOS1, NAV2, NCALD, NLRP3, NPRL3, OPRL1, OXT, P2RY2, PCSK5, PER2, PKP2, QRFP, SERPING1, SLC19A1, SLC22A5, SLC24A3, SLC44A1, SLC5A6, SLC6A6, SLC8A1, SLCO3A1, SMAD3, SRC, TBC1D8, TBXAS1, TMIGD3, WNK1, WWTR1, YES1 |
| GO:0030234 | enzyme regulator activity | 0.00 | 10.34 | 142.00 | ABR, ACAP1, AGAP2, AGAP7P, AKAP13, AKT1, ALOX5AP, ANKRD27, ANKRD54, ANXA3, ANXA5, ARAP1, ARAP2, ARHGAP15, ARHGAP17, ARHGAP21, ARHGAP22, ARHGAP26, ARHGAP27, ARHGAP31, ARHGEF10L, ARHGEF26, ARHGEF28, ATP2A3, ATP2B4, AZIN2, BCR, BIN1, BMPR1B, BST2, CAB39, CABIN1, CARD14, CCND3, CCPG1, CHN1, CRIM1, DAXX, DENND1A, DENND3, DENND4A, DLC1, DOCK1, DOCK4, EFNA5, EIF2S1, ESR1, ETFDH, FARP2, FGD4, FNIP1, FRY, GNA12, GNB5, GPS1, IPO7, IQGAP2, ITGB1BP1, ITSN2, LAMTOR3, LGALS3, LMTK2, MAL, MAPK8, MCF2L2, MET, MRAP, NF1, NLRP3, NOL3, NOTCH1, NPRL3, NRP1, PCOLCE2, PHACTR3, PHACTR4, PIK3R1, PIK3R5, PINX1, PISD, PLCE1, PNKD, PPP1R37, PPP4R3B, PPP6R3, PREX1, PRKAR1B, PRKAR2A, PRKCE, PRPSAP1, RABGAP1, RABGEF1, RALGAPA2, RALGAPB, RAP1GAP, RAPGEF4, RASA3, RASGEF1A, RCAN1, RCC2, RGS3, RGS6, RGS9, RIN2, RINL, RNH1, SCG5, SERPINA1, SERPINF1, SERPING1, SH3RF2, SIPA1, SIPA1L1, SIPA1L3, SKI, SLC19A1, SLX4, SOCS3, SPINK6, SPINT1, SPRED2, SRC, STAP1, STARD13, SYNGAP1, TAB1, TAOK1, TBC1D1, TBC1D14, TBC1D22B, TBC1D8, TBCD, TESC, TIMP2, TNK2, TRAF4, UBE2O, UNC45A, VAV3, WASL, WNK1, ZEB2 |
| GO:0000902 | cell morphogenesis | 0.00 | 10.25 | 113.00 | ABI2, ABL1, ACTN4, ADD1, ANKRD27, ANTXR1, ARAP1, ARHGAP15, ARHGEF26, ARHGEF28, ASXL1, ATP10A, B4GALT5, BCL11A, BMPR1B, CDC42EP3, CDH10, CDH12, CDH2, CFDP1, CHN1, CLU, CNTN5, COL18A1, CORO1C, CPNE6, CUX1, CUX2, DAG1, DIP2B, DLC1, DOCK1, DTNBP1, ECE1, EEF2K, EFNA5, EIF2AK4, EPHA1, EPHB6, EXT1, FGD4, FRY, GAS7, GNA12, GP1BA, HEG1, ITGB1BP1, ITSN2, LATS2, LIMS1, LMTK2, LRP2, MACF1, MAP1S, MAPK14, MBP, MERTK, MET, MFSD2A, MKLN1, MRAP, NBL1, NDEL1, NEK3, NOL3, NOTCH1, NR4A2, NRP1, P2RX7, PACSIN2, PAK6, PALM, PDZD8, PIK3R1, PREX1, PRKCZ, PRMT3, PXDN, PXN, RADIL, RCC2, RDX, RHOBTB3, RREB1, RUFY3, S100B, SCRIB, SDC2, SEMA3C, SEMA4B, SEMA6B, SHTN1, SIPA1L1, SIPA1L3, SLIT1, SMURF1, SNX1, SPP1, SRC, SS18L2, SSH1, SYNGAP1, TAOK1, TBCD, TMEFF1, TMEM108, TNN, UBE3A, ULK1, VDR, WASL, ZFPM1, ZNF365 |
| GO:0051336 | regulation of hydrolase activity | 0.00 | 10.11 | 110.00 | ABL1, ABR, AGAP2, AGAP7P, AKT1, ANTXR1, ARAP1, ARAP2, ARHGAP15, ARHGAP22, ARHGAP27, ARHGEF26, ASPH, ATP2A3, BCR, BIN1, BST2, CASP10, CCL22, CCPG1, CHN1, CORO1C, CRADD, CRIM1, CTSB, DAP, DENND1A, DLC1, DNAJB6, EFNA5, EIF2S1, EPHA1, ESR1, FADD, FGD4, FNIP1, GNA12, GNB5, GRAMD4, IQGAP2, ITGA6, ITGB1BP1, LGALS3, LIMS1, LPIN1, LRCH1, MAL, MAPK7, MAPK8, MBP, MEFV, MET, MRAP, MYC, NANOS1, NDEL1, NF1, NLRP3, NOL3, NTRK3, PCOLCE2, PCSK5, PCSK6, PDZD2, PKP4, PML, POR, PPP6R3, PREX1, PRKCZ, RABGAP1, RALGAPA2, RALGAPB, RAP1GAP, RAPGEF4, RASA3, RASGEF1A, RCAN1, RCC2, RDX, RGS6, RGS9, S100A8, SCARB2, SCRIB, SERPINA1, SERPINF1, SERPING1, SIPA1, SIPA1L1, SIPA1L3, SLC39A10, SMAD3, SORL1, SORT1, SPINK6, SPINT1, SRC, SYNGAP1, TBC1D1, TBC1D14, TBC1D22B, TBC1D8, TIMP2, TP63, TRAPPC6A, UBE2O, USP47, VAV3, WNK1 |

**Supplementary Table 4:** Significantly enriched GO-Biological Processes enriched using the progressively hypomethylated (Down trending) genes during the period of gestation.