

## SUPPLEMENTARY TABLES

**Supplementary Table 1. Blood physiological and biochemical indicators in young, adult, and old groups.**

| Project          | Young group    | Adult group    | Old group      | P       | Young vs Adult | Young vs Old | Adult vs Old |
|------------------|----------------|----------------|----------------|---------|----------------|--------------|--------------|
| WBC ( $10^9/L$ ) | 6.135±0.21     | 7.552±0.39     | 6.035±0.32     | 0.002** | 0.002**        | 0.797        | 0.001**      |
| Neu% (%)         | 66.55±2.84     | 75.594±1.93    | 78.058±0.83    | 0.000** | 0.007**        | 0.000**      | 0.456        |
| Lym% (%)         | 25.692±0.95    | 17.381±1.09    | 17.642±0.78    | 0.000** | 0.000**        | 0.000**      | 0.854        |
| Mon% (%)         | 3.362±0.3      | 3.275±0.43     | 2.942±0.38     | 0.666   | 0.873          | 0.386        | 0.545        |
| Bas% (%)         | 0.323±0.047    | 0.213±0.043    | 0.192±0.046    | 0.090   | 0.119          | 0.039*       | 0.771        |
| Neu ( $10^9/L$ ) | 4.338±0.207    | 5.711±0.34     | 4.841±0.231    | 0.002** | 0.000**        | 0.131        | 0.024*       |
| Lym ( $10^9/L$ ) | 1.539±0.061    | 1.265±0.089    | 1.089±0.068    | 0.000** | 0.011*         | 0.000**      | 0.103        |
| Mon ( $10^9/L$ ) | 0.158±0.02     | 0.174±0.041    | 0.124±0.022    | 0.404   | 0.686          | 0.323        | 0.207        |
| Bas ( $10E9/L$ ) | 0.017±0.002    | 0.014±0.003    | 0.006±0.001    | 0.001** | 0.501          | 0.000**      | 0.011*       |
| RBC (g/L)        | 5.926±0.075    | 6.235±0.161    | 5.962±0.111    | 0.150   | 0.063          | 0.803        | 0.107        |
| HGB (g/L)        | 118.286±1.52   | 125.438±3.773  | 115.04±1.996   | 0.013*  | 0.037*         | 0.274        | 0.003**      |
| HCT (%)          | 30.882±0.404   | 32.525±0.997   | 30.248±0.574   | 0.054   | 0.076          | 0.431        | 0.017*       |
| MCV (fL)         | 52.096±0.316   | 52.056±0.415   | 50.74±0.397    | 0.015*  | 0.943          | 0.008**      | 0.025*       |
| MCH (pg)         | 19.968±0.12    | 20.081±0.151   | 19.316±0.148   | 0.000** | 0.590          | 0.001**      | 0.001**      |
| MCHC (g/L)       | 383.357±0.814  | 385.875±0.995  | 380.8±1.238    | 0.009** | 0.114          | 0.068        | 0.002**      |
| RDW-CV (%)       | 14.954±0.152   | 14.556±0.177   | 15.044±0.19    | 0.181   | 0.137          | 0.698        | 0.075        |
| RDW -SD (fL)     | 34.4±0.462     | 33.419±0.491   | 33.72±0.546    | 0.392   | 0.207          | 0.318        | 0.703        |
| PLT ( $10^9/L$ ) | 455.571±22.536 | 356.063±25.348 | 313.28±23.89   | 0.000** | 0.008**        | 0.000**      | 0.251        |
| MPV (fL)         | 5.079±0.049    | 5.263±0.138    | 5.748±0.181    | 0.001** | 0.353          | 0.000**      | 0.018*       |
| PDW (fL)         | 14.625±0.035   | 14.881±0.08    | 15.116±0.142   | 0.001** | 0.087          | 0.000**      | 0.124        |
| PCT (%)          | 0.232±0.012    | 0.186±0.014    | 0.174±0.012    | 0.002** | 0.019*         | 0.001**      | 0.513        |
| TBIL (umol/L)    | 1.818±0.119    | 2.331±0.235    | 1.923±0.127    | 0.072   | 0.025*         | 0.591        | 0.077        |
| DBIL (umol/L)    | 0.286±0.029    | 0.35±0.055     | 0.292±0.047    | 0.572   | 0.317          | 0.906        | 0.375        |
| IDBIL (umol/L)   | 1.532±0.128    | 1.981±0.222    | 1.631±0.128    | 0.140   | 0.052          | 0.618        | 0.132        |
| TP (g/L)         | 62.404±0.642   | 65.744±1.175   | 65.8±0.73      | 0.003** | 0.007**        | 0.002**      | 0.963        |
| ALB (g/L)        | 33.675±0.355   | 30.988±0.502   | 31.346±0.432   | 0.000** | 0.000**        | 0.000**      | 0.581        |
| GLO (g/L)        | 28.729±0.515   | 34.756±1.101   | 34.454±0.839   | 0.000** | 0.000**        | 0.000**      | 0.801        |
| A/G              | 1.186±0.023    | 0.9±0.034      | 0.931±0.032    | 0.000** | 0.000**        | 0.000**      | 0.501        |
| AST (U/L)        | 56.429±1.968   | 63.313±2.625   | 70.654±2.538   | 0.000** | 0.059          | 0.000**      | 0.047*       |
| ALT (U/L)        | 112.975±4.614  | 83.456±6.834   | 85.85±5.01     | 0.000** | 0.000**        | 0.000**      | 0.769        |
| ST/LT            | 0.516±0.023    | 0.822±0.062    | 0.868±0.042    | 0.000** | 0.000**        | 0.000**      | 0.449        |
| GGT (U/L)        | 6.571±0.274    | 5.75±0.512     | 10.654±1.124   | 0.000** | 0.487          | 0.000**      | 0.000**      |
| ALP (U/L)        | 212.393±14.908 | 111.438±9.854  | 125.038±8.302  | 0.000** | 0.000**        | 0.000**      | 0.473        |
| LDH (U/L)        | 603.458±46.008 | 629.667±87.027 | 609.348±66.661 | 0.962   | 0.786          | 0.945        | 0.834        |
| PAB (mg/L)       | 13.536±1.425   | 13.525±1.848   | 20.392±8.168   | 0.572   | 0.999          | 0.339        | 0.411        |

|               |                 |                |               |         |         |         |        |
|---------------|-----------------|----------------|---------------|---------|---------|---------|--------|
| ADA (U/L)     | 5.004±0.302     | 4.431±0.355    | 5.212±0.309   | 0.284   | 0.243   | 0.624   | 0.118  |
| CHE (U/L)     | 1288.393±53.706 | 1005.188±55.89 | 1145.538±45.1 | 0.002** | 0.001** | 0.041*  | 0.084  |
| 5-NT (U/L)    | 2.179±0.272     | 1.994±0.301    | 1.954±0.226   | 0.797   | 0.648   | 0.524   | 0.923  |
| AFU (U/L)     | 3.536±0.145     | 3.744±0.27     | 4.546±0.232   | 0.001** | 0.513   | 0.000** | 0.015* |
| TBA (umol/L)  | 41.457±5.794    | 28.419±6.929   | 39.827±5.376  | 0.327   | 0.154   | 0.836   | 0.217  |
| BUN (mmol/L)  | 4.6±0.251       | 4.207±0.341    | 4.302±0.221   | 0.545   | 0.326   | 0.390   | 0.815  |
| Cr (umol/L)   | 99.093±4.467    | 108.819±5.651  | 116.938±7.015 | 0.079   | 0.281   | 0.025*  | 0.375  |
| UA (umol/L)   | 26.25±2.619     | 32.625±3.64    | 29.269±2.581  | 0.335   | 0.144   | 0.423   | 0.446  |
| BMG (mg/L)    | 0.357±0.062     | 0.479±0.094    | 0.465±0.098   | 0.529   | 0.349   | 0.338   | 0.919  |
| CYS-C (mg/L)  | 0.051±0.005     | 0.129±0.07     | 0.052±0.007   | 0.144   | 0.074   | 0.998   | 0.078  |
| K (mmol/L)    | 5.087±0.085     | 4.763±0.2      | 4.975±0.086   | 0.171   | 0.061   | 0.452   | 0.223  |
| Na (mmol/L)   | 126.411±0.437   | 125.85±0.679   | 124.804±0.511 | 0.068   | 0.480   | 0.022*  | 0.195  |
| CL (mmol/L)   | 96.089±0.443    | 94.956±0.703   | 93.25±0.477   | 0.000** | 0.151   | 0.000** | 0.035* |
| TG (mmol/L)   | 1.544±0.092     | 1.911±0.097    | 2.098±0.097   | 0.000** | 0.015   | 0.000** | 0.215  |
| CHOL (mmol/L) | 5.594±0.183     | 4.841±0.28     | 5.728±0.358   | 0.115   | 0.086   | 0.723   | 0.047* |
| HDL (mmol/L)  | 3.769±0.076     | 2.945±0.111    | 3.019±0.096   | 0.000** | 0.000** | 0.000** | 0.602  |
| LDL (mmol/L)  | 3.312±0.137     | 2.846±0.223    | 3.463±0.258   | 0.161   | 0.149   | 0.586   | 0.060  |
| APOA1 (g/L)   | 0.696±0.021     | 0.632±0.03     | 0.66±0.022    | 0.187   | 0.077   | 0.245   | 0.447  |
| APOB (g/L)    | 0.02±0.002      | 0.032±0.005    | 0.033±0.003   | 0.008** | 0.019*  | 0.004** | 0.867  |
| FMN (mmol/L)  | 1.46±0.039      | 1.446±0.044    | 1.447±0.039   | 0.961   | 0.821   | 0.804   | 0.991  |
| GLU (mmol/L)  | 4.671±0.115     | 4.581±0.267    | 4.01±0.137    | 0.006** | 0.707   | 0.002** | 0.022* |

Note: Most common used hematologic and biochemical parameters were tested. The marked \* was significant difference ( $P<0.05$ ), and the marked \*\* was extremely significant difference ( $P<0.01$ ). The unmarked letter indicated no statistical difference.

**Supplementary Table 2. Comparison between the original data of transcriptional and the reference genome.**

| Sample | Total-reads | Total-map        | Unique-map       | Multi-map      |
|--------|-------------|------------------|------------------|----------------|
| M01    | 73761706    | 65238878(88.45%) | 63195124(85.67%) | 2043754(2.77%) |
| F01    | 88047074    | 78826105(89.53%) | 76378332(86.75%) | 2447773(2.78%) |
| M03    | 73432368    | 66498999(90.56%) | 63964670(87.11%) | 2534329(3.45%) |
| M07    | 70987850    | 64093554(90.29%) | 62370381(87.86%) | 1723173(2.43%) |
| F08    | 99443568    | 89609460(90.11%) | 86429246(86.91%) | 3180214(3.2%)  |
| F12    | 81912444    | 73484901(89.71%) | 70953267(86.62%) | 2531634(3.09%) |
| M28    | 85232600    | 77444526(90.86%) | 73071227(85.73%) | 4373299(5.13%) |
| F28    | 84586998    | 75216823(88.92%) | 71049159(84.0%)  | 4167664(4.93%) |

**Supplementary Table 3. Each profile significantly enriched in the KEGG pathway.**

| KEGG_Name                               | Corrected P-Value | Input   | Profile |
|---|-------------------|---|---------|
| Adherens junction                       | 0.041             | MET TCF7 LEF1 SMAD3                                 |         |
| Gastric cancer                          | 0.041             | MET TCF7 LEF1 SHC2 SMAD3                            |         |
| Pathways in cancer                      | 0.041             | TCF7 PIM2 ESR2 SMAD3 MET FOXO1 TRAF4 LEF1<br> FGFR3 | 0       |
| Hepatocellular carcinoma                | 0.041             | MET TCF7 LEF1 SHC2 SMAD3                            |         |
| B cell receptor signaling pathway       | 0.0001            | CR2 CD72 CD22 CD19 BLNK CD79B CD79A                 | Profile |
| Primary immunodeficiency                | 0.005             | CD79A BLNK TNFRSF13C CD19                           | 1       |
| p53 signaling pathway                   | 0.0007            | GTSE1 CCNB1 CCNE1 RRM2                              | Profile |
| Cell cycle                              | 0.003             | CCNB1 MCM4 BUB1 CCNE1                               |         |
| Oocyte meiosis                          | 0.028             | CCNB1 CCNE1 BUB1                                    | 3       |
| ECM-receptor interaction                | 0.002             | ITGA2B ITGB3 VWF GP1BB                              |         |
| Hematopoietic cell lineage              | 0.002             | EPOR ITGA2B ITGB3 GP1BB                             |         |
| Platelet activation                     | 0.004             | ITGA2B ITGB3 VWF GP1BB                              |         |
| Complement and coagulation cascades     | 0.013             | VWF C1QC C1QA                                       |         |
| Focal adhesion                          | 0.014             | ITGA2B ITGB3 MYL5 VWF                               | Profile |
| Porphyrin and chlorophyll metabolism    | 0.024             | BLVRB ALAS2   | 4       |
| Prion diseases                          | 0.029             | C1QC C1QA   |         |
| Human papillomavirus infection          | 0.042             | ITGA2B ITGB3 ISG15 VWF                              |         |
| Staphylococcus aureus infection         | 0.042             | C1QC C1QA   |         |
| PI3K-Akt signaling pathway              | 0.049             | EPOR ITGA2B ITGB3 VWF                               |         |
| Cytokine-cytokine receptor interaction  | 0.006             | LIF CXCL2 CXCL8 BMPR1A CXCL10 IL1R2 IL1R1           |         |
| Amoebiasis                              | 0.019             | CXCL8 IL1R2 IL1R1 LAMA5                             | Profile |
| Transcriptional misregulation in cancer | 0.019             | GADD45A SPINT1 IL1R2 ETV7 CXCL8                     | 6       |

**Supplementary Table 4. WGBS raw data quality control statistics.**

| Sample name | Raw_reads | clean_reads | Clean_ratio(%) | Q20(%) | Q30(%) | GC(%) | BS conversion rate(%) |
|-------------|-----------|-------------|----------------|--------|--------|-------|-----------------------|
| F01         | 348184904 | 342475648   | 88.16          | 97.63  | 92.33  | 22.34 | 99.495                |
| M01         | 346787724 | 341261170   | 89.03          | 97.62  | 92.28  | 22.18 | 99.596                |
| M03         | 364891330 | 359118399   | 89.12          | 97.65  | 92.38  | 22.24 | 99.606                |
| M07         | 356155312 | 350566471   | 88.84          | 97.49  | 92.00  | 22.40 | 99.611                |
| F08         | 331811447 | 327684301   | 90.18          | 97.52  | 91.87  | 21.94 | 99.721                |
| F12         | 325285795 | 321201535   | 88.65          | 97.82  | 92.83  | 22.24 | 99.542                |
| M28         | 343875597 | 335720363   | 87.31          | 97.10  | 91.11  | 22.22 | 99.554                |
| F28         | 347389962 | 339694259   | 88.15          | 96.92  | 90.66  | 22.00 | 99.672                |

**Supplementary Table 5. The statistics of methylation status of c-site.**

| sample | C_covgMean | C(Mb)   | CG(Mb) | CHG(Mb) | CHH(Mb) | MeanC(%) | MeanCG(%) | MeanCHG(%) | MeanCHH(%) |
|--------|------------|---------|--------|---------|---------|----------|-----------|------------|------------|
| F01    | 10.4       | 9745.2  | 565.1  | 2070.9  | 7109.2  | 5.31     | 80.21     | 0.66       | 0.71       |
| M01    | 11.2       | 10471.3 | 605.2  | 2224.8  | 7641.4  | 5.21     | 80.85     | 0.56       | 0.57       |
| M03    | 11.6       | 10795.8 | 625.0  | 2299.3  | 7871.5  | 5.20     | 80.74     | 0.55       | 0.57       |
| M07    | 11.5       | 10708.3 | 625.6  | 2285.0  | 7797.7  | 5.12     | 79.24     | 0.52       | 0.52       |
| F08    | 11.4       | 10677.2 | 593.1  | 2244.6  | 7839.5  | 4.98     | 81.03     | 0.52       | 0.50       |
| F12    | 10.3       | 9608.6  | 557.9  | 2043.8  | 7006.9  | 5.25     | 80.12     | 0.62       | 0.64       |
| M28    | 10.4       | 9670.9  | 556.7  | 2059.7  | 7054.5  | 5.20     | 80.06     | 0.61       | 0.64       |
| F28    | 11.1       | 10413.5 | 597.2  | 2210.9  | 7605.4  | 5.02     | 79.47     | 0.49       | 0.49       |