**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  | 75.94±1.93  | 78.05±0.83| 0.000**| 0.007**        | 0.000**      | 0.456        |
| Lym% (%)     | 25.69±0.95  | 17.38±1.09  | 17.64±0.78| 0.000**| 0.000**        | 0.000**      | 0.854        |
| Mon% (%)     | 3.36±0.3    | 3.27±0.43   | 2.94±0.38 | 0.666  | 0.873          | 0.386        | 0.545        |
| Bas% (%)     | 0.32±0.047  | 0.21±0.043  | 0.19±0.046| 0.090  | 0.119          | 0.039*       | 0.771        |
| Neu (10^9/L)| 4.33±0.207  | 5.71±0.34   | 4.84±0.231| 0.002**| 0.000**        | 0.131        | 0.024*       |
| Lym (10^9/L) | 1.53±0.061  | 1.26±0.089  | 1.08±0.068| 0.000**| 0.011*         | 0.000**      | 0.103        |
| Mon (10^9/L) | 0.15±0.02   | 0.17±0.041  | 0.12±0.022| 0.404  | 0.686          | 0.323        | 0.207        |
| Bas (10E9/L) | 0.01±0.002  | 0.01±0.003  | 0.006±0.001| 0.001**| 0.501          | 0.000**      | 0.011*       |
| RBC (g/L)    | 5.92±0.075  | 6.23±0.161  | 5.96±0.111| 0.150  | 0.063          | 0.803        | 0.107        |
| HGB (g/L)    | 118.28±1.52 | 125.43±3.73 | 115.04±1.996| 0.013*| 0.037*         | 0.274        | 0.003**      |
| HCT (%)      | 30.88±0.404 | 32.52±0.997 | 30.24±0.574| 0.054  | 0.076          | 0.431        | 0.017*       |
| MCV (fl)     | 52.09±0.316 | 52.05±0.415 | 50.74±0.397| 0.015*| 0.943          | 0.008**      | 0.025*       |
| MCH (pg)     | 19.96±0.12  | 20.08±0.151 | 19.31±0.148| 0.000**| 0.590         | 0.001**      | 0.001**      |
| MCHC (g/L)   | 383.35±0.814| 385.87±0.995| 380.8±1.238| 0.009**| 0.114          | 0.068        | 0.002**      |
| RDW-CV (%)   | 14.95±0.152 | 14.56±0.177 | 15.04±0.19 | 0.181 | 0.137          | 0.698        | 0.075        |
| RDW-SD (fl)  | 34.4±0.462  | 33.41±0.491 | 33.72±0.546| 0.392  | 0.207          | 0.318        | 0.703        |
| PLT (10^9/L) | 455.57±22.536| 356.06±25.348| 313.28±23.89| 0.000**| 0.008**        | 0.000**      | 0.251        |
| MPV (fl)     | 5.07±0.049  | 5.26±0.138  | 5.74±0.181| 0.001**| 0.353          | 0.000**      | 0.018*       |
| PDW (fl)     | 14.62±0.35  | 14.88±0.08  | 15.11±0.142| 0.001**| 0.087          | 0.000**      | 0.124        |
| PCT (%)      | 0.23±0.012  | 0.18±0.014  | 0.17±0.012| 0.002**| 0.019*         | 0.001**      | 0.513        |
| TBIL (umol/L)| 1.81±0.119  | 2.33±0.235  | 1.92±0.127| 0.072  | 0.025*         | 0.591        | 0.077        |
| DBIL (umol/L)| 0.28±0.029  | 0.35±0.055  | 0.29±0.047| 0.572  | 0.317          | 0.906        | 0.375        |
| IDBIL (umol/L) | 1.53±0.128  | 1.98±0.222  | 1.63±0.128| 0.140  | 0.052          | 0.618        | 0.132        |
| TP (g/L)     | 62.40±0.642 | 65.74±1.175 | 65.8±0.73 | 0.003**| 0.007**        | 0.002**      | 0.963        |
| ALB (g/L)    | 33.67±0.355 | 30.98±0.502 | 31.34±0.432| 0.000**| 0.000**        | 0.000**      | 0.581        |
| GLO (g/L)    | 28.72±0.515 | 34.75±1.101 | 34.45±0.839| 0.000**| 0.000**        | 0.000**      | 0.801        |
| A/G          | 1.18±0.023  | 0.9±0.034   | 0.93±0.032| 0.000**| 0.000**        | 0.000**      | 0.501        |
| AST (U/L)    | 56.42±1.968 | 63.31±2.625 | 70.65±2.538| 0.000**| 0.059          | 0.000**      | 0.047*       |
| ALT (U/L)    | 112.97±4.614| 83.45±6.834 | 85.85±5.01| 0.000**| 0.000**        | 0.000**      | 0.769        |
| ST/LT        | 0.51±0.023  | 0.82±0.062  | 0.86±0.042| 0.000**| 0.000**        | 0.000**      | 0.449        |
| GGT (U/L)    | 6.57±0.274  | 5.75±0.512  | 10.65±1.124| 0.000**| 0.487          | 0.000**      | 0.000**      |
| ALP (U/L)    | 212.39±14.908| 111.43±9.854| 125.03±8.302| 0.000**| 0.000**        | 0.000**      | 0.473        |
| LDH (U/L)    | 603.45±46.008| 629.66±87.027| 609.34±66.661| 0.962 | 0.786          | 0.945        | 0.834        |
| PAB (mg/L)   | 13.53±1.425 | 13.52±1.848 | 20.39±8.168| 0.572  | 0.999          | 0.339        | 0.411        |
| Parameter   | 1st Value       | 2nd Value       | 3rd Value       | 4th Value       | 5th Value       | 6th Value       | 7th Value       |
|-------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 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%) |
| 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(84.00%) | 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       | Profile 0 |
| Gastric cancer                   | 0.041             | MET|TCF7|LEF1|SHC2|SMAD3       |         |
| Pathways in cancer               | 0.041             | TCF7|PIM2|ESR2|SMAD3|MET|FOXO1|TRAF4|LEF1|FGFR3     |         |
| Hepatocellular carcinoma         | 0.041             | MET|TCF7|LEF1|SHC2|SMAD3       |         |
| B cell receptor signaling pathway| 0.0001            | CR2|CD72|CD22|CD19|BLNK|CD79B|CD79A|CD79A|BLNK|TNFRSF13C|CD19     | Profile 1 |
| Primary immunodeficiency         | 0.005             | CCNB1|MCM4|BUB1|CCNE1       |         |
| p53 signaling pathway            | 0.0007            | GTSE1|CCNB1|CCNE1|RRM2       |         |
| Cell cycle                       | 0.003             | CCNB1|MCM4|BUB1|CCNE1       |         |
| Oocyte meiosis                   | 0.028             | CCNB1|CCNE1|BUB1       |         |
| 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       |         |
| Porphyrin and chlorophyll metabolism| 0.024          | BLVRB|ALAS2      |         |
| 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      |         |
| Transcriptional misregulation in cancer | 0.019     | GADD45A|SPINT1|IL1R2|ETV7|CXCL8    |         |
**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        |