Supplementary files for
Integration of transcriptome and methylome highlights the roles of cell cycle and hippo signaling pathway in fish sexual size dimorphism

Na Wang a, b, c*, Qian Yang a, d, Jialin Wang a, d, Rui Shi a, d, Ming Li a, b, Jin Gao d, Wenteng Xu a, b, Yingming Yang a, b, c, Yadong Chen a, b, Songlin Chen a, b*

a Key Laboratory for Sustainable Development of Marine Fisheries, Ministry of Agriculture and Rural Affairs, Yellow Sea Fisheries Research Institute, Chinese Academy of Fishery Sciences, Qingdao 266071, China
b Laboratory for Marine Fisheries Science and Food Production Processes, Qingdao National Laboratory for Marine Science and Technology, Qingdao 266235, China
c Shandong Key Laboratory of Marine Fisheries Biotechnology and Genetic Breeding, Qingdao 266071, China
d College of Fisheries and Life Science, Shanghai Ocean University, Shanghai 201306, China
e Hainan Academy of Ocean and Fisheries Sciences, Haikou 570203, China

*Correspondence:
Profs. Na Wang and Songlin Chen
Yellow Sea Fisheries Research Institute
Chinese Academy of Fishery Sciences
106 Nanjing Road
Qingdao 266071, China
Tel: (+86)-532-85831605;
Fax: (+86)-532-85811514;
Email: wangna@ysfri.ac.cn; chensl@ysfri.ac.cn
Figure S1. The reads filter statistics in the whole transcriptomic analysis.
Figure S2. The PCA analysis for the whole transcriptome.
Figure S3. The top 20 GO terms in the brain.
Figure S4. The top 20 GO terms in the liver.
Figure S5. The top 20 GO terms in the gonad.
Figure S6. The top 20 GO terms in the muscle.
Figure S7. The genes’ expression pattern in the turquoise and brown modules and their relationship between module membership and gene significance for body weight.
Figure S8. The GO terms enrichment in the turquoise module.
Figure S9. The GO terms enrichment in the brown module.
Figure S10. The sequencing depth and coverage analysis in WGBS.
Figure S11. The expression pattern of important epigenetic regulatory factors.
Figure S12. The demonstration of DMRs in the methylome and their functional KEGG enrichment analysis.
Figure S13. The KEGG enrichment analysis for the DMGs.
Figure S14. The Spearman's correlation between DNA methylation and gene expression within the samples.
Figure S15. The overlapped genes in DMGs and DEGs, and their trends calculation.

Table S1. The reads information in the whole transcriptomic analysis.
Table S2. The KEGG enrichment in four tissues.
Table S3. The sample growth trait used in WGCNA.
Table S4. The primers used in present study.
Table S5. The sequencing data information in the WGBS.
Table S6. The genomic DNA methylation levels in 18 samples.
Figure S1. The reads filter statistics in the whole transcriptomic analysis.
Figure S2. The PCA analysis for the whole transcriptome.
Figure S3. The top 20 GO terms in the brain.

**A.** Top 20 GO terms in MB-vs-FB

| ID          | Description                                           |
|-------------|-------------------------------------------------------|
| GO:0051179  | localization                                          |
| GO:0044765  | single-organism transport                             |
| GO:0068111  | ion transport                                         |
| GO:0033036  | macromolecule localization                           |
| GO:0008810  | transport                                             |
| GO:1902578  | single-organism localization                         |
| GO:0051234  | establishment of localization                        |
| GO:0301554  | cell differentiation                                  |
| GO:0432228  | non-membrane-bound organelle                         |
| GO:0432322  | intracellular non-membrane-bound organelle           |
| GO:0044446  | organelle part                                       |
| GO:0068159  | protein binding                                      |
| GO:022899   | substrate-specific transporter activity               |
| GO:009215   | transporter activity                                  |
| GO:046914   | transition metal ion binding                          |
| GO:015075   | ion transmembrane transporter activity                |
| GO:003876   | nucleic acid binding                                 |
| GO:022891   | substrate-specific transmembrane transporter activity |
| GO:022857   | transmembrane transporter activity                    |

**B.** Top 20 GO terms in MB-vs-PMB

| ID          | Description                                           |
|-------------|-------------------------------------------------------|
| GO:0044237  | cellular metabolic process                            |
| GO:0044238  | primary metabolic process                             |
| GO:0006807  | nitrogen compound metabolic process                   |
| GO:0006464  | cellular protein modification process                 |
| GO:1901360  | organic cyclic compound metabolic process             |
| GO:0036211  | protein modification process                          |
| GO:0067304  | nucleic acid metabolic process                        |
| GO:006725   | cellular aromatic compound metabolic process          |
| GO:0061399  | nucleobase-containing compound metabolic process      |
| GO:008152   | metabolic process                                     |
| GO:043412   | macromolecule modification                            |
| GO:019870   | PNA metabolic process                                 |
| GO:046843   | heterocycle metabolic process                         |
| GO:036796   | phosphate-containing compound metabolic process        |
| GO:034641   | cellular nitrogen compound metabolic process          |
| GO:0067933  | phosphorus metabolic process                          |
| GO:005448   | binding                                               |
| GO:0043169  | cation binding                                        |
| GO:0066914  | transition metal ion binding                          |
| GO:0016787  | hydrolase activity                                    |

**C.** Top 20 GO terms in PMB-vs-FB

| ID          | Description                                           |
|-------------|-------------------------------------------------------|
| GO:0044765  | single-organism transport                             |
| GO:1902578  | single-organism localization                         |
| GO:006461   | protein complex assembly                              |
| GO:0305856  | cytoskeleton                                          |
| GO:044446   | intracellular organelle part                          |
| GO:019870   | microtubule cytoskeleton                              |
| GO:004440   | cytoskeletal part                                     |
| GO:031988   | membrane-bound vesicle                                |
| GO:031982   | vesicle                                               |
| GO:004428   | nuclear part                                          |
| GO:005834   | nucleus                                               |
| GO:0043228  | non-membrane-bound organelle                         |
| GO:0043232  | intracellular non-membrane-bound organelle            |
| GO:0044422  | organelle part                                       |
| GO:0044429  | ubiquitin–like protein ligase binding                 |
| GO:004462   | phosphatase activity                                 |
| GO:0168181  | hydrolase activity, acting on acid anhydrides, in phosphorus-containing anhydrides |
| GO:016817   | hydrolase activity, acting on acid anhydrides         |
| GO:008989   | enzyme binding                                        |
| GO:0031588  | structural molecule activity                          |
Figure S4. The top 20 GO terms in the liver.

A) Top 20 GO terms in ML-vs-FL

| ID             | Description                                                                 |
|----------------|-----------------------------------------------------------------------------|
| GO:005179      | localization                                                                |
| GO:0051234     | establishment of localization                                               |
| GO:0006810     | transport                                                                   |
| GO:0006796     | phosphate-containing compound metabolic process                             |
| GO:0006793     | phosphorus metabolic process                                                |
| GO:1902578     | single-organism localization                                                |
| GO:0044765     | single-organism transport                                                  |
| GO:0019338     | protein metabolic process                                                  |
| GO:006464      | cellular protein modification process                                        |
| GO:036211      | protein modification process                                                |
| GO:0031323     | regulation of cellular metabolic process                                    |
| GO:0043412     | macromolecule modification                                                  |
| GO:0080090     | regulation of primary metabolic process                                     |
| GO:0044238     | primary metabolic process                                                  |
| GO:0016788     | hydrolase activity, acting on ester bonds                                   |
| GO:0003824     | catalytic activity                                                          |
| GO:0097159     | organic cyclic compound binding                                             |
| GO:0048914     | transition metal ion binding                                                |
| GO:0016787     | hydrolase activity                                                          |
| GO:0016773     | transferase activity, transferring phosphorus-containing groups             |

B) Top 20 GO terms in ML-vs-PML

| ID             | Description                                                                 |
|----------------|-----------------------------------------------------------------------------|
| GO:0008152     | metabolic process                                                           |
| GO:0044238     | primary metabolic process                                                   |
| GO:0044710     | single-organism metabolic process                                           |
| GO:006796      | phosphate-containing compound metabolic process                             |
| GO:0044249     | intracellular part                                                          |
| GO:009922      | intracellular                                                               |
| GO:009923      | cell                                                                         |
| GO:004464      | cell part                                                                   |
| GO:0043226     | organelle                                                                   |
| GO:0043229     | intracellular organelle                                                     |
| GO:0043227     | membrane-bounded organelle                                                  |
| GO:0043231     | intracellular membrane-bounded organelle                                    |
| GO:0043228     | non-membrane-bounded organelle                                              |
| GO:0043232     | intracellular non-membrane-bounded organelle                                |
| GO:0003824     | catalytic activity                                                          |
| GO:0043167     | ion binding                                                                 |
| GO:0043189     | cation binding                                                              |
| GO:0046814     | transition metal ion binding                                                |
| GO:0016787     | hydrolase activity                                                          |
| GO:0046872     | metal ion binding                                                           |

C) Top 20 GO terms in PML-vs-FL

| ID             | Description                                                                 |
|----------------|-----------------------------------------------------------------------------|
| GO:0070857     | cellular response to chemical stimulus                                      |
| GO:0019335     | response to organic substance                                               |
| GO:0019310     | cellular response to organic substance                                      |
| GO:0043221     | response to chemical                                                        |
| GO:0007049     | cell cycle                                                                  |
| GO:0016798     | hydrolase activity, acting on glycosyl bonds                                |
| GO:0003824     | catalytic activity                                                          |
| GO:0016787     | hydrolase activity                                                          |
| GO:0070111     | peptidase activity, acting on L-amino acid peptides                         |
| GO:004175      | endopeptidase activity                                                      |
| GO:0016791     | phosphatase activity                                                        |
| GO:008233      | peptidase activity                                                          |
| GO:0016491     | cytochrome activity                                                         |
| GO:0042578     | phosphoester hydrolase activity                                             |
| GO:0016788     | hydrolase activity, acting on ester bonds                                   |
| GO:0044872     | receptor activity                                                           |
| GO:0008219     | transporter activity                                                         |
| GO:0008283     | signaling receptor activity                                                 |
| GO:0004871     | signal transducer activity                                                  |
| GO:0069089     | molecular transducer activity                                               |
Figure S5. The top 20 GO terms in the gonad.

A) Top 20 GO terms in MG-vs-FG

B) Top 20 GO terms in MG-vs-PMG

C) Top 20 GO terms in PMG-vs-FG
Figure S6. The top 20 GO terms in the muscle.

### Top 20 GO terms in MM-vs-FM

| ID          | Description                                      |
|-------------|--------------------------------------------------|
| GO:0006259  | DNA metabolic process                            |
| GO:0006204  | nucleic acid metabolic process                   |
| GO:0006725  | cellular aromatic compound metabolic process     |
| GO:0006139  | nucleobase-containing compound metabolic process |
| GO:0046483  | heterocycle metabolic process                    |
| GO:1901360  | organic cyclic compound metabolic process        |
| GO:0034641  | cellular nitrogen compound metabolic process      |
| GO:0006807  | nitrogen compound metabolic process              |
| GO:0006896  | organelle organization                           |
| GO:0043228  | non-membrane-bounded organelle                   |
| GO:0043232  | intracellular non-membrane-bounded organelle     |
| GO:0044446  | intracellular organelle part                     |
| GO:0043229  | organelle part                                   |
| GO:005623   | cell                                             |
| GO:004464   | cell part                                        |
| GO:0043226  | organelle                                       |
| GO:005622   | intracellular                                   |
| GO:0044424  | intracellular part                               |
| GO:0005623  | cell                                             |
| GO:004464   | cell part                                        |
| GO:0044444  | cytoplasmic part                                 |
| GO:005673   | cytoplasm                                       |
| GO:0043228  | non-membrane-bounded organelle                   |
| GO:0043232  | intracellular non-membrane-bounded organelle     |

### Top 20 GO terms in MM-vs-PMM

| ID          | Description                                      |
|-------------|--------------------------------------------------|
| GO:0071704  | organic substance metabolic process              |
| GO:0043170  | macromolecule metabolic process                  |
| GO:0051179  | localization                                     |
| GO:0052924  | establishment of localization                    |
| GO:0039293  | developmental process                            |
| GO:0044767  | single-organism developmental process            |
| GO:0032501  | multicellular organometabolic process            |
| GO:0044707  | single-multicellular organometabolic process     |
| GO:0044424  | intracellular part                               |
| GO:0005622  | intracellular                                   |
| GO:0043229  | intracellular organelle                          |
| GO:0043226  | organelle                                       |
| GO:0043231  | intracellular membrane-bounded organelle         |
| GO:0043227  | membrane-bounded organelle                       |
| GO:005623   | cell                                             |
| GO:004464   | cell part                                        |
| GO:0044444  | cytoplasmic part                                 |
| GO:005673   | cytoplasm                                       |
| GO:0043228  | non-membrane-bounded organelle                   |
| GO:0043232  | intracellular non-membrane-bounded organelle     |

### Top 20 GO terms in PMM-vs-FM

| ID          | Description                                      |
|-------------|--------------------------------------------------|
| GO:0006204  | nucleic acid metabolic process                   |
| GO:0006725  | cellular aromatic compound metabolic process     |
| GO:1901360  | organic cyclic compound metabolic process        |
| GO:0006139  | nucleobase-containing compound metabolic process |
| GO:0046483  | heterocycle metabolic process                    |
| GO:0006807  | nitrogen compound metabolic process              |
| GO:0006896  | organelle organization                           |
| GO:0034641  | cellular nitrogen compound metabolic process      |
| GO:0006807  | nitrogen compound metabolic process              |
| GO:0043228  | non-membrane-bounded organelle                   |
| GO:0043232  | intracellular non-membrane-bounded organelle     |
| GO:0044446  | intracellular organelle part                     |
| GO:0044422  | organelle part                                   |
| GO:0043229  | intracellular organelle                          |
| GO:0043226  | organelle                                       |
| GO:005623   | cell                                             |
| GO:004464   | cell part                                        |
| GO:0044444  | cytoplasmic part                                 |
| GO:005673   | cytoplasm                                       |
| GO:0043228  | non-membrane-bounded organelle                   |
| GO:0043232  | intracellular non-membrane-bounded organelle     |
| GO:0016462  | pyrophosphatase activity                         |
Figure S7. The genes’ expression pattern in the turquoise and brown modules and their relationship between module membership and gene significance for body weight.
Figure S8. The GO terms enrichment in the turquoise module.
Figure S9. The GO terms enrichment in the brown module.
Figure S10. The sequencing depth and coverage analysis in WGBS.
Figure S11. The expression pattern of important epigenetic regulatory factors.
Figure S12. The demonstration of DMRs in the methylome and their functional KEGG enrichment analysis.
Figure S13. The KEGG enrichment analysis for the DMGs.
Figure S14. The Spearman's correlation between DNA methylation and gene expression within the samples.
Figure S15. The overlapped genes in DMGs and DEGs, and their trends calculation.
Table S1. The reads information in the whole transcriptomi analysis.

| Sample | RawData | CleanData (%) | Adapter (%) | LowQuality (%) | polyA (%) | N (%) | CleanData |
|--------|---------|---------------|-------------|----------------|-----------|-------|-----------|
| FB1    | 94811290 | 94510580 (99.68%) | 102736 (0.11%) | 197792 (0.21%) | 0 (0.00%) | 182 (0.00%) | 94510580 |
| FB2    | 82084128 | 81845872 (99.71%) | 77302 (0.09%) | 160782 (0.20%) | 0 (0.00%) | 172 (0.00%) | 81845872 |
| FB3    | 74231542 | 74030202 (99.73%) | 48412 (0.07%) | 152928 (0.21%) | 0 (0.00%) | 0 (0.00%) | 74030202 |
| FG1    | 137107874 | 136876838 (99.83%) | 58314 (0.04%) | 172722 (0.13%) | 0 (0.00%) | 0 (0.00%) | 136876838 |
| FG2    | 97318682 | 97195282 (99.87%) | 29112 (0.03%) | 94272 (0.10%) | 0 (0.00%) | 16 (0.00%) | 97195282 |
| FG3    | 81040072 | 80898190 (99.82%) | 26858 (0.03%) | 115024 (0.14%) | 0 (0.00%) | 0 (0.00%) | 80898190 |
| FL1    | 75427550 | 75288994 (99.82%) | 27904 (0.04%) | 110652 (0.15%) | 0 (0.00%) | 0 (0.00%) | 75288994 |
| FL2    | 91339940 | 91160896 (99.80%) | 33480 (0.04%) | 145548 (0.16%) | 0 (0.00%) | 16 (0.00%) | 91160896 |
| FL3    | 75135958 | 75055356 (99.89%) | 15632 (0.02%) | 64806 (0.09%) | 0 (0.00%) | 164 (0.00%) | 75055356 |
| FM1    | 96499476 | 96316920 (99.81%) | 46252 (0.05%) | 136300 (0.14%) | 0 (0.00%) | 4 (0.00%) | 96316920 |
| FM2    | 78431672 | 78254342 (99.76%) | 50234 (0.06%) | 136096 (0.17%) | 0 (0.00%) | 0 (0.00%) | 78254342 |
| FM3    | 92414456 | 92190890 (99.76%) | 68880 (0.07%) | 154686 (0.17%) | 0 (0.00%) | 0 (0.00%) | 92190890 |
| MB1    | 75406168 | 75182548 (99.70%) | 60234 (0.08%) | 163386 (0.22%) | 0 (0.00%) | 0 (0.00%) | 75182548 |
| MB2    | 81316698 | 81051236 (99.67%) | 73472 (0.08%) | 191990 (0.24%) | 0 (0.00%) | 0 (0.00%) | 81051236 |
| MB3    | 78486654 | 78281698 (99.74%) | 61030 (0.08%) | 143766 (0.18%) | 0 (0.00%) | 160 (0.00%) | 78281698 |
| MG1    | 82980228 | 82778660 (99.76%) | 51838 (0.06%) | 149730 (0.18%) | 0 (0.00%) | 0 (0.00%) | 82778660 |
| MG2    | 80336438 | 80110742 (99.72%) | 59842 (0.07%) | 165854 (0.21%) | 0 (0.00%) | 0 (0.00%) | 80110742 |
| MG3    | 90271024 | 90055304 (99.76%) | 48574 (0.05%) | 167144 (0.19%) | 0 (0.00%) | 2 (0.00%) | 90055304 |
| ML1    | 80121430 | 79968532 (99.81%) | 35824 (0.04%) | 116838 (0.15%) | 0 (0.00%) | 236 (0.00%) | 79968532 |
| ML2    | 96400226 | 96250984 (99.85%) | 32416 (0.03%) | 116818 (0.12%) | 0 (0.00%) | 8 (0.00%) | 96250984 |
| ML3    | 74008444 | 73882874 (99.83%) | 27832 (0.04%) | 97738 (0.13%) | 0 (0.00%) | 0 (0.00%) | 73882874 |
| MM1    | 83387898 | 83242796 (99.83%) | 35416 (0.04%) | 109686 (0.13%) | 0 (0.00%) | 0 (0.00%) | 83242796 |
| MM2    | 98864352 | 98676840 (99.81%) | 40722 (0.04%) | 146790 (0.15%) | 0 (0.00%) | 0 (0.00%) | 98676840 |
| MM3    | 223195894 | 222800826 (99.82%) | 99166 (0.04%) | 295458 (0.13%) | 0 (0.00%) | 444 (0.00%) | 222800826 |
| PMB1   | 175465318 | 174938822 (99.70%) | 137498 (0.08%) | 388998 (0.22%) | 0 (0.00%) | 0 (0.00%) | 174938822 |
| PMB2   | 73684006 | 73444742 (99.68%) | 66708 (0.09%) | 172556 (0.23%) | 0 (0.00%) | 0 (0.00%) | 73444742 |
| PMB3   | 83210960 | 83003298 (99.75%) | 61914 (0.07%) | 145556 (0.17%) | 0 (0.00%) | 192 (0.00%) | 83003298 |
| Sample | OD280 Val | OD260 Val | OD250 Val | OD230 Val | OD180 Val | OD220 Val |
|--------|-----------|-----------|-----------|-----------|-----------|-----------|
| PMG1   | 70916372  | 70739318  | 32244     | 144046    | 0         | 764       |
| PMG2   | 79364636  | 79156814  | 48714     | 159108    | 0         | 0         |
| PMG3   | 170060420 | 169579072 | 111992    | 369356    | 0         | 0         |
| PML1   | 83503244  | 83353394  | 34556     | 115102    | 0         | 192       |
| PML2   | 90939358  | 90838162  | 17890     | 83300     | 0         | 6         |
| PML3   | 94437886  | 94211768  | 75426     | 150682    | 0         | 10        |
| PMM1   | 99168972  | 98974518  | 46942     | 147266    | 0         | 246       |
| PMM2   | 100678354 | 100516610 | 34612     | 126942    | 0         | 190       |
| PMM3   | 87379998  | 87223556  | 36346     | 119886    | 0         | 210       |
Table S2. The KEGG enrichment in four tissues.

| Groups       | ID      | Description                                  | Pvalue     | Qvalue     | Up    | Down   | fg_num | bg_num |
|--------------|---------|-----------------------------------------------|------------|------------|-------|--------|--------|--------|
| MG-vs-FG     | ko04110 | Cell cycle                                    | 2.90E-05   | 0.009964   | 74    | 30     | 104    | 145    |
| MG-vs-FG     | ko05322 | Systemic lupus erythematosus                  | 0.00044    | 0.0548     | 31    | 19     | 50     | 66     |
| MG-vs-FG     | ko04610 | Complement, serine and threonine metabolism   | 0.00048    | 0.0548     | 5     | 37     | 42     | 54     |
| MG-vs-FG     | ko00260 | Glycine, serine and threonine metabolism      | 0.00142    | 0.122397   | 17    | 16     | 33     | 42     |
| MG-vs-FG     | ko00053 | Ascorbate and aldarate metabolism             | 0.00379    | 0.209123   | 9     | 11     | 20     | 24     |
| MG-vs-FG     | ko00240 | Pyrimidine metabolism                          | 0.00439    | 0.209123   | 46    | 25     | 71     | 104    |
| MG-vs-FG     | ko03013 | RNA transport                                  | 0.00457    | 0.209123   | 71    | 40     | 111    | 170    |
| MG-vs-FG     | ko05216 | Thyroid cancer                                 | 0.00486    | 0.209123   | 17    | 20     | 37     | 50     |
| MG-vs-FG     | ko04218 | Cellular senescence                           | 0.00593    | 0.226781   | 64    | 78     | 142    | 223    |
| MG-vs-FG     | ko03030 | DNA replication                                | 0.00873    | 0.275885   | 24    | 2      | 26     | 34     |
| MG-vs-FG     | ko04115 | p53 signaling pathway                          | 0.00882    | 0.275885   | 38    | 22     | 60     | 88     |
| MG-vs-FG     | ko00010 | Glycolysis / Gluconeogenesis                   | 0.01288    | 0.32574    | 22    | 30     | 52     | 76     |
| MG-vs-FG     | ko05150 | Staphylococcus aureus infection                | 0.01308    | 0.32574    | 3     | 29     | 32     | 44     |
| MG-vs-FG     | ko00340 | Histidine metabolism                           | 0.01326    | 0.32574    | 11    | 6      | 17     | 21     |
| MG-vs-FG     | ko03440 | Homologous recombination                       | 0.02065    | 0.439776   | 22    | 5      | 27     | 37     |
| MG-vs-FG     | ko03320 | PPAR signaling pathway                         | 0.02109    | 0.439776   | 21    | 32     | 53     | 79     |
| MG-vs-FG     | ko05206 | MicroRNAs in cancer                            | 0.02423    | 0.439776   | 61    | 73     | 134    | 216    |
| MG-vs-FG     | ko05222 | Small cell lung cancer                         | 0.02435    | 0.439776   | 38    | 37     | 75     | 116    |
| MG-vs-FG     | ko01100 | Metabolic pathways                             | 0.02445    | 0.439776   | 410   | 396    | 806    | 1398   |
| MG-vs-FG     | ko00982 | Drug metabolism - cytochrome P450              | 0.02557    | 0.439776   | 8     | 13     | 21     | 28     |
| MG-vs-FG     | ko04512 | ECM-receptor interaction                       | 0.02705    | 0.443144   | 10    | 54     | 64     | 98     |
| MG-vs-FG     | ko00983 | Drug metabolism - other enzymes                | 0.02923    | 0.45699    | 18    | 21     | 39     | 57     |
| MG-vs-FG     | ko05161 | Hepatitis B                                    | 0.03445    | 0.490631   | 49    | 50     | 99     | 158    |
| MG-vs-FG     | ko00564 | Glycerophospholipid metabolism                 | 0.03473    | 0.490631   | 21    | 52     | 73     | 114    |
| MG-vs-FG     | ko05214 | Glioma                                        | 0.03617    | 0.490631   | 30    | 28     | 58     | 89     |
| MG-vs-FG     | ko05034 | Alcoholism                                     | 0.03708    | 0.490631   | 58    | 49     | 107    | 172    |
| MG-vs-FG     | ko00920 | Sulfur metabolism                             | 0.0397     | 0.492077   | 2     | 6      | 8      | 9      |
| Condition                                      | Pathway                                  | MG-vs-FG  | PMG-vs-FG  |
|-----------------------------------------------|------------------------------------------|-----------|------------|
| Colorectal cancer                             |                                          | 0.02033   | 0.709956   |
| p53 signaling pathway                         |                                          | 0.04110   | 0.492077   |
| Thyroid cancer                                |                                          | 0.02107   | 0.709956   |
| Systemic lupus erythematosus                  |                                          | 0.00018   | 0.030692   |
| Pyrimidine metabolism                         |                                          | 0.00135   | 0.154898   |
| Arachidonic acid metabolism                   |                                          | 0.00218   | 0.186705   |
| Histidine metabolism                          |                                          | 0.00347   | 0.206172   |
| Complement and coagulation cascades           |                                          | 0.00361   | 0.206172   |
| Hepatitis B                                   |                                          | 0.00466   | 0.228116   |
| p53 signaling pathway                         |                                          | 0.00962   | 0.379703   |
| Glycine, serine and threonine metabolism      |                                          | 0.01096   | 0.379703   |
| Thyroid cancer                                |                                          | 0.01191   | 0.379703   |
| Ascorbate and aldarate metabolism             |                                          | 0.014001  | 0.379703   |
| Pathway                        | Score1  | Score2          | FDR 1  | FDR 2  | N1    | N2    | N3    | N4    |
|-------------------------------|---------|-----------------|--------|--------|-------|-------|-------|-------|
| Prostate cancer               | 0.01401 | 0.379703        | 35     | 51     | 86    | 132   |       |       |
| Cellular senescence           | 0.01439 | 0.379703        | 63     | 77     | 140   | 223   |       |       |
| ECM-receptor interaction      | 0.01779 | 0.435939        | 10     | 55     | 65    | 98    |       |       |
| PPAR signaling pathway        | 0.02267 | 0.460502        | 19     | 34     | 53    | 79    |       |       |
| DNA replication               | 0.02335 | 0.460502        | 24     | 1      | 25    | 34    |       |       |
| Small cell lung cancer        | 0.02654 | 0.460502        | 37     | 38     | 75    | 116   |       |       |
| Drug metabolism - cytochrome P450 | 0.02665 | 0.460502        | 7      | 14     | 21    | 28    |       |       |
| MicroRNAs in cancer           | 0.02727 | 0.460502        | 62     | 72     | 134   | 216   |       |       |
| Arginine and proline metabolism | 0.02933 | 0.460502        | 20     | 16     | 36    | 52    |       |       |
| Drug metabolism - other enzymes | 0.03098 | 0.460502        | 17     | 22     | 39    | 57    |       |       |
| Acute myeloid leukemia        | 0.03463 | 0.460502        | 23     | 28     | 51    | 77    |       |       |
| Cholesterol metabolism        | 0.03559 | 0.460502        | 15     | 25     | 40    | 59    |       |       |
| Transcriptional misregulation in cancers | 0.03735 | 0.460502        | 51     | 75     | 126   | 204   |       |       |
| Glycerophospholipid metabolism | 0.03764 | 0.460502        | 22     | 51     | 73    | 114   |       |       |
| Metabolic pathways            | 0.03852 | 0.460502        | 404    | 401    | 805   | 1398  |       |       |
| RNA transport                 | 0.03856 | 0.460502        | 65     | 41     | 106   | 170   |       |       |
| Hematopoietic cell lineage    | 0.03875 | 0.460502        | 12     | 43     | 55    | 84    |       |       |
| Protein digestion and absorption | 0.03893 | 0.460502        | 15     | 68     | 83    | 131   |       |       |
| Sulfur metabolism             | 0.04057 | 0.463865        | 2      | 6      | 8     | 9     |       |       |
| Bladder cancer                | 0.0457  | 0.490127        | 21     | 10     | 31    | 45    |       |       |
| B cell receptor signaling pathway | 0.04697 | 0.490127        | 11     | 40     | 51    | 78    |       |       |
| Homologous recombination      | 0.04716 | 0.490127        | 22     | 4      | 26    | 37    |       |       |
| Oocyte meiosis                | 0.00141 | 0.316191        | 8      | 0      | 8     | 126   |       |       |
| Pathogenic Escherichia coli infection | 0.00437 | 0.36709         | 3      | 5      | 8     | 151   |       |       |
| Ubiquitin mediated proteolysis | 0.00492 | 0.36709         | 7      | 1      | 8     | 154   |       |       |
| Cell cycle                    | 0.01226 | 0.579657        | 6      | 1      | 7     | 145   |       |       |
| Apoptosis                     | 0.01294 | 0.579657        | 5      | 3      | 8     | 182   |       |       |
| Amino sugar and nucleotide sugar metabolism | 0.02274 | 0.848985        | 3      | 1      | 4     | 63    |       |       |
| Ubiquinone and other terpenoid-quinone biosynthesis | 0.03005 | 0.888856        | 2      | 0      | 2     | 16    |       |       |
| Nucleotide excision repair    | 0.0329  | 0.888856        | 0      | 3      | 3     | 41    |       |       |
| Dataset       | KEGG ID       | Description                                              | p-value | Z-score | Number of genes | FDR-corrected p-value |
|--------------|---------------|----------------------------------------------------------|---------|---------|-----------------|-----------------------|
| MB-vs-FB     | ko00250       | Alanine, aspartate and glutamate metabolism             | 0.03939 | 0.88886 | 3               | 0                     |
| MB-vs-FB     | ko05012       | Parkinson disease                                        | 0.0442  | 0.88886 | 5               | 1                     |
| MB-vs-PMB    | ko04120       | Ubiquitin mediated proteolysis                           | 0.003   | 0.30366 | 6               | 1                     |
| MB-vs-PMB    | ko00524       | Neomycin, kanamycin and gentamicin biosynthesis          | 0.0031  | 0.30366 | 1               | 1                     |
| MB-vs-PMB    | ko05012       | Parkinson disease                                        | 0.01086 | 0.56752 | 5               | 1                     |
| MB-vs-PMB    | ko03420       | Nucleotide excision repair                               | 0.0142  | 0.56752 | 0               | 3                     |
| MB-vs-PMB    | ko00360       | Phenylalanine metabolism                                 | 0.01851 | 0.60456 | 2               | 0                     |
| MB-vs-PMB    | ko03018       | RNA degradation                                          | 0.02383 | 0.66723 | 3               | 1                     |
| MB-vs-PMB    | ko01200       | Carbon metabolism                                       | 0.02863 | 0.70137 | 2               | 3                     |
| MB-vs-PMB    | ko00520       | Amino sugar and nucleotide sugar metabolism             | 0.04353 | 0.93339 | 2               | 1                     |
| PMB-vs-FB    | ko05130       | Pathogenic Escherichia coli infection                    | 0.00095 | 0.08303 | 1               | 4                     |
| PMB-vs-FB    | ko00232       | Caffeine metabolism                                     | 0.01527 | 0.46301 | 0               | 1                     |
| PMB-vs-FB    | ko02010       | ABC transporters                                         | 0.01597 | 0.46301 | 0               | 2                     |
| PMB-vs-FB    | ko04540       | Gap junction                                             | 0.02405 | 0.46586 | 0               | 3                     |
| PMB-vs-FB    | ko05216       | Thyroid cancer                                           | 0.02677 | 0.46586 | 1               | 1                     |
| PMB-vs-FB    | ko04145       | Phagosome                                                | 0.04421 | 0.64104 | 0               | 3                     |
| ML-vs-FL     | ko00910       | Nitrogen metabolism                                     | 0.0087  | 0.67971 | 2               | 1                     |
| ML-vs-FL     | ko04972       | Pancreatic secretion                                     | 0.016   | 0.67971 | 4               | 3                     |
| ML-vs-FL     | ko04110       | Cell cycle                                               | 0.01905 | 0.67971 | 6               | 1                     |
| ML-vs-FL     | ko00030       | Pentose phosphate pathway                                | 0.02339 | 0.67971 | 2               | 1                     |
| ML-vs-FL     | ko04120       | Ubiquitin mediated proteolysis                           | 0.02553 | 0.67971 | 7               | 0                     |
| ML-vs-FL     | ko05214       | Glioma                                                   | 0.02557 | 0.67971 | 2               | 3                     |
| ML-vs-FL     | ko05225       | Hepatocellular carcinoma                                | 0.03003 | 0.67971 | 4               | 4                     |
| ML-vs-FL     | ko00520       | Amino sugar and nucleotide sugar metabolism             | 0.03014 | 0.67971 | 3               | 1                     |
| ML-vs-FL     | ko04114       | Oocyte meiosis                                           | 0.03085 | 0.67971 | 6               | 0                     |
| ML-vs-FL     | ko05224       | Breast cancer                                            | 0.03247 | 0.67971 | 4               | 4                     |
| ML-vs-FL     | ko04914       | Progesterone-mediated oocyte maturation                  | 0.03269 | 0.67971 | 5               | 0                     |
| ML-vs-FL     | ko04142       | Lysosome                                                 | 0.03531 | 0.67971 | 5               | 2                     |
| ML-vs-FL     | ko05220       | Chronic myeloid leukemia                                 | 0.04548 | 0.71347 | 2               | 3                     |
| Comparison  | KEGG Pathway                        | p-value 1 | p-value 2 | num1 | num2 | num3 | num4 |
|------------|-------------------------------------|-----------|-----------|------|------|------|------|
| ML-vs-FL   | ko00730 Thiamine metabolism         | 0.04852   | 0.713475  | 1    | 1    | 2    | 19   |
| ML-vs-FL   | ko00250 Alanine, aspartate and glutamate metabolism | 0.04897   | 0.713475  | 3    | 0    | 3    | 44   |
| ML-vs-PML  | ko04972 Pancreatic secretion        | 0.00029   | 0.063766  | 4    | 4    | 8    | 140  |
| ML-vs-PML  | ko00059 Linoleic acid metabolism    | 0.00106   | 0.092116  | 1    | 2    | 3    | 17   |
| ML-vs-PML  | ko00592 alpha-Linolenic acid metabolism | 0.00126  | 0.092116  | 1    | 2    | 3    | 18   |
| ML-vs-PML  | ko00010 Glycolysis / Gluconeogenesis | 0.00227  | 0.109124  | 0    | 5    | 5    | 76   |
| ML-vs-PML  | ko04975 Fat digestion and absorption | 0.00248  | 0.109124  | 1    | 3    | 4    | 47   |
| ML-vs-PML  | ko05012 Parkinson disease           | 0.00983   | 0.310524  | 5    | 1    | 6    | 150  |
| ML-vs-PML  | ko04120 Ubiquitin mediated proteolysis | 0.01111  | 0.310524  | 6    | 0    | 6    | 154  |
| ML-vs-PML  | ko00564 Glycerophospholipid metabolism | 0.01254  | 0.310524  | 3    | 2    | 5    | 114  |
| ML-vs-PML  | ko00561 Glycerolipid metabolism     | 0.01623   | 0.310524  | 2    | 2    | 4    | 80   |
| ML-vs-PML  | ko0250 Alanine, aspartate and glutamate metabolism | 0.01623  | 0.310524  | 3    | 0    | 3    | 44   |
| ML-vs-PML  | ko00590 Arachidonic acid metabolism | 0.01623  | 0.310524  | 1    | 2    | 3    | 44   |
| ML-vs-PML  | ko04270 Vascular smooth muscle contraction | 0.01694  | 0.310524  | 4    | 2    | 6    | 169  |
| ML-vs-PML  | ko00565 Ether lipid metabolism       | 0.02162   | 0.365825  | 1    | 2    | 3    | 49   |
| ML-vs-PML  | ko01100 Metabolic pathways           | 0.02626   | 0.387432  | 12   | 13   | 25   | 1398 |
| ML-vs-PML  | ko01200 Carbon metabolism            | 0.02642   | 0.387432  | 1    | 4    | 5    | 138  |
| ML-vs-PML  | ko00910 Nitrogen metabolism          | 0.03155   | 0.43379   | 1    | 1    | 2    | 23   |
| ML-vs-PML  | ko00520 Amino sugar and nucleotide sugar metabolism | 0.04128  | 0.534204  | 2    | 1    | 3    | 63   |
| PML-vs-FL  | ko03320 PPAR signaling pathway       | 0.0001    | 0.014376  | 2    | 3    | 5    | 79   |
| PML-vs-FL  | ko00500 Starch and sucrose metabolism | 0.00128  | 0.088775  | 2    | 1    | 3    | 36   |
| PML-vs-FL  | ko00730 Thiamine metabolism         | 0.00571   | 0.264412  | 1    | 1    | 2    | 19   |
| PML-vs-FL  | ko01100 Metabolic pathways           | 0.01427   | 0.391252  | 9    | 6    | 15   | 1398 |
| PML-vs-FL  | ko04115 p53 signaling pathway        | 0.01579   | 0.391252  | 1    | 2    | 3    | 88   |
| PML-vs-FL  | ko00790 Folate biosynthesis          | 0.01768   | 0.391252  | 1    | 1    | 2    | 34   |
| PML-vs-FL  | ko00052 Galactose metabolism         | 0.0197    | 0.391252  | 2    | 0    | 2    | 36   |
| PML-vs-FL  | ko00250 Alanine, aspartate and glutamate metabolism | 0.0287   | 0.400739  | 1    | 1    | 2    | 44   |
| PML-vs-FL  | ko05162 Measles                      | 0.029     | 0.400739  | 0    | 3    | 3    | 111  |
| PML-vs-FL  | ko05222 Small cell lung cancer       | 0.03245   | 0.400739  | 2    | 1    | 3    | 116  |
| PML-vs-FL  | ko01212 Fatty acid metabolism        | 0.03767   | 0.400739  | 2    | 0    | 2    | 51   |
| Pathway ID   | Pathway Name                                           | Adjusted p-value | q-value | Downregulated Genes | Upregulated Genes | Total Genes |
|-------------|--------------------------------------------------------|------------------|---------|---------------------|-------------------|-------------|
| ko04973     | Carbohydrate digestion and absorption                 | 0.03903          | 0.400739|                     |                   | 2 0 2 52    |
| ko05206     | MicroRNAs in cancer                                   | 0.04049          | 0.400739|                     |                   | 2 2 4 216   |
| ko00524     | Neomycin, kanamycin and gentamicin biosynthesis       | 0.0415           | 0.400739|                     |                   | 1 0 1 7     |
| ko04974     | Protein digestion and absorption                      | 0.04406          | 0.400739|                     |                   | 3 0 3 131   |
| ko04340     | Hedgehog signaling pathway                            | 0.04905          | 0.400739|                     |                   | 1 1 2 59    |
| ko04979     | Cholesterol metabolism                                | 0.04905          | 0.400739|                     |                   | 1 1 2 59    |
| ko04110     | Cell cycle                                            | 1.59E-17         | 5.02E-15| 52 1 53 145         |                   |            |
| ko05322     | Systemic lupus erythematosus                          | 7.01E-08         | 1.10E-05| 19 4 23 66          |                   |            |
| ko03030     | DNA replication                                        | 4.0E-07          | 4.20E-05| 15 0 15 34          |                   |            |
| ko03460     | Fanconi anemia pathway                                | 2.87E-06         | 2.26E-04| 18 0 18 53          |                   |            |
| ko04914     | Progesterone-mediated oocyte maturation               | 7.34E-06         | 4.42E-04| 25 0 25 95          |                   |            |
| ko04114     | Oocyte meiosis                                        | 8.42E-06         | 4.42E-04| 27 3 30 126         |                   |            |
| ko04218     | Cellular senescence                                   | 1.52E-05         | 6.85E-04| 29 15 44 223        |                   |            |
| ko03440     | Homologous recombination                              | 4.62E-05         | 1.82E-03| 13 0 13 37          |                   |            |
| ko03430     | Mismatch repair                                       | 0.00074          | 2.23E-02| 8 0 8 21            |                   |            |
| ko03040     | Spliceosome                                           | 0.00076          | 2.23E-02| 25 1 26 131         |                   |            |
| ko00240     | Pyrimidine metabolism                                 | 0.00078          | 2.23E-02| 19 3 22 104         |                   |            |
| ko05034     | Alcoholism                                            | 0.00135          | 3.55E-02| 28 3 31 172         |                   |            |
| ko03018     | RNA degradation                                       | 0.00334          | 8.09E-02| 18 0 18 88          |                   |            |
| ko00061     | Fatty acid biosynthesis                                | 0.01047          | 2.36E-01| 4 1 5 14            |                   |            |
| ko05216     | Thyroid cancer                                        | 0.01149          | 2.41E-01| 7 4 11 50           |                   |            |
| ko05213     | Endometrial cancer                                    | 0.01402          | 2.68E-01| 11 4 15 79          |                   |            |
| ko04120     | Ubiquitin mediated proteolysis                        | 0.01444          | 2.68E-01| 23 2 25 154         |                   |            |
| ko04115     | p53 signaling pathway                                 | 0.01699          | 2.97E-01| 16 0 16 88          |                   |            |
| ko00982     | Drug metabolism - cytochrome P450                      | 0.02081          | 3.35E-01| 4 3 7 28            |                   |            |
| ko03420     | Nucleotide excision repair                            | 0.02159          | 3.35E-01| 9 0 9 41            |                   |            |
| ko00320     | Purine metabolism                                     | 0.02231          | 3.35E-01| 28 4 32 216         |                   |            |
| ko03013     | RNA transport                                         | 0.0259           | 3.71E-01| 22 4 26 170         |                   |            |
| ko03022     | Basal transcription factors                           | 0.03712          | 5.08E-01| 8 0 8 38            |                   |            |
| ko04540     | Gap junction                                          | 0.04404          | 5.49E-01| 12 7 19 122         |                   |            |
| Condition                        | Pathway                                                      | p-value 1   | p-value 2   | q-value 1 | q-value 2 | n1  | n2  | n   | n   |
|--------------------------------|--------------------------------------------------------------|-------------|-------------|-----------|-----------|-----|-----|-----|-----|
| MM-vs-FM                       | Herpes simplex infection                                    | 0.04475     | 5.49E-01    | 24        | 3         | 27  | 187 |     |     |
| MM-vs-FM                       | Colorectal cancer                                            | 0.04727     | 5.49E-01    | 15        | 4         | 19  | 123 |     |     |
| MM-vs-FM                       | Base excision repair                                        | 0.04791     | 5.49E-01    | 7         | 0         | 7   | 33  |     |     |
| MM-vs-PMM                      | Renin-angiotensin system                                    | 0.00221     | 0.263915    | 2         | 1         | 3   | 19  |     |     |
| MM-vs-PMM                      | Vascular smooth muscle contraction                           | 0.0025      | 0.263915    | 6         | 2         | 8   | 169 |     |     |
| MM-vs-PMM                      | Ubiquitin mediated proteolysis                               | 0.00579     | 0.336218    | 6         | 1         | 7   | 154 |     |     |
| MM-vs-PMM                      | Alzheimer disease                                            | 0.00845     | 0.336218    | 7         | 1         | 8   | 207 |     |     |
| MM-vs-PMM                      | cGMP - PKG signaling pathway                                 | 0.0094      | 0.336218    | 8         | 1         | 9   | 255 |     |     |
| MM-vs-PMM                      | Protein digestion and absorption                             | 0.01009     | 0.336218    | 6         | 0         | 6   | 131 |     |     |
| MM-vs-PMM                      | ECM-receptor interaction                                    | 0.01201     | 0.336218    | 4         | 1         | 5   | 98  |     |     |
| MM-vs-PMM                      | Focal adhesion                                              | 0.01275     | 0.336218    | 6         | 3         | 9   | 268 |     |     |
| MM-vs-PMM                      | Protein processing in endoplasmic reticulum                 | 0.01464     | 0.343235    | 4         | 3         | 7   | 184 |     |     |
| MM-vs-PMM                      | Parkinson disease                                           | 0.01866     | 0.393751    | 5         | 1         | 6   | 150 |     |     |
| MM-vs-PMM                      | Adherens junction                                           | 0.03988     | 0.762802    | 4         | 1         | 5   | 134 |     |     |
| MM-vs-PMM                      | Renin secretion                                             | 0.04711     | 0.762802    | 3         | 1         | 4   | 97  |     |     |
| MM-vs-PMM                      | Hedgehog signaling pathway                                  | 0.04963     | 0.762802    | 1         | 2         | 3   | 59  |     |     |
| PMM-vs-FM                      | Cell cycle                                                  | 1.54E-19    | 4.72E-17    | 49        | 0         | 49  | 145 |     |     |
| PMM-vs-FM                      | DNA replication                                             | 1.10E-08    | 1.69E-06    | 15        | 0         | 15  | 34  |     |     |
| PMM-vs-FM                      | Systemic lupus erythematosus                                | 8.34E-08     | 8.54E-06    | 17        | 3         | 20  | 66  |     |     |
| PMM-vs-FM                      | Homologous recombination                                    | 8.68E-05     | 6.53E-03    | 11        | 0         | 11  | 37  |     |     |
| PMM-vs-FM                      | Oocyte meiosis                                              | 0.00011     | 6.53E-03    | 22        | 1         | 23  | 126 |     |     |
| PMM-vs-FM                      | Progesterone-mediated oocyte maturation                      | 0.00013     | 6.53E-03    | 19        | 0         | 19  | 95  |     |     |
| PMM-vs-FM                      | Pyrimidine metabolism                                       | 0.00015     | 6.61E-03    | 17        | 3         | 20  | 104 |     |     |
| PMM-vs-FM                      | p53 signaling pathway                                       | 0.00044     | 1.68E-02    | 16        | 1         | 17  | 88  |     |     |
| PMM-vs-FM                      | Mismatch repair                                             | 0.00081     | 2.75E-02    | 7         | 0         | 7   | 21  |     |     |
| PMM-vs-FM                      | Cellular senescence                                         | 0.00263     | 7.74E-02    | 25        | 5         | 30  | 223 |     |     |
| PMM-vs-FM                      | Proximal tubule bicarbonate reclamation                     | 0.00277     | 7.74E-02    | 7         | 2         | 9   | 39  |     |     |
| PMM-vs-FM                      | MicroRNAs in cancer                                         | 0.00317     | 8.10E-02    | 26        | 3         | 29  | 216 |     |     |
| PMM-vs-FM                      | Mucin type O-glycan biosynthesis                            | 0.00757     | 1.57E-01    | 7         | 0         | 7   | 30  |     |     |
| PMM-vs-FM                      | Bladder cancer                                              | 0.00759     | 1.57E-01    | 8         | 1         | 9   | 45  |     |     |
| Category                        | Pathway                                   | p-value | E-value | Count | Group 1 | Group 2 | Total |
|--------------------------------|-------------------------------------------|---------|---------|-------|---------|---------|-------|
| PMM-vs-FM                      | ko03460 Fanconi anemia pathway             | 0.00766 | 1.57E-01| 10    | 0       | 10      | 53    |
| PMM-vs-FM                      | ko03018 RNA degradation                    | 0.00861 | 1.65E-01| 14    | 0       | 14      | 88    |
| PMM-vs-FM                      | ko03420 Nucleotide excision repair        | 0.01342 | 2.42E-01| 8     | 0       | 8       | 41    |
| PMM-vs-FM                      | ko05034 Alcoholism                         | 0.01618 | 2.76E-01| 20    | 2       | 22      | 172   |
| PMM-vs-FM                      | ko01524 Platinum drug resistance          | 0.02233 | 3.61E-01| 10    | 0       | 10      | 62    |
| PMM-vs-FM                      | ko00910 Nitrogen metabolism               | 0.03085 | 4.73E-01| 4     | 1       | 5       | 23    |
| PMM-vs-FM                      | ko00230 Purine metabolism                 | 0.03348 | 4.89E-01| 21    | 4       | 25      | 216   |
| PMM-vs-FM                      | ko05216 Thyroid cancer                    | 0.04053 | 5.59E-01| 6     | 2       | 8       | 50    |
| PMM-vs-FM                      | ko03410 Base excision repair              | 0.04191 | 5.59E-01| 6     | 0       | 6       | 33    |
| PMM-vs-FM                      | ko00601 Lysosphingolipid biosynthesis - lacto and neolacto series | 0.04946 | 6.15E-01| 7     | 0       | 7       | 43    |
Table S3. The sample growth traits used in WGCNA.

| Sample | Sample Body length (Average) | Body length for three individuals | Sample Body width (Average) | Body width for three individuals | Sample Body weight (Average) | Body weight for three individuals |
|--------|------------------------------|----------------------------------|-----------------------------|---------------------------------|------------------------------|---------------------------------|
| FB1    | 51.00                        | 47.00; 54.00; 52.00              | 15.50                       | 16.00; 15.50; 15.00             | 857.27                      | 917.00; 846.10; 808.70          |
| FB2    | 52.17                        | 53.00; 50.50; 53.00              | 15.00                       | 16.00; 15.50; 15.00             | 775.33                      | 903.00; 727.00; 696.00          |
| FB3    | 51.00                        | 49.00; 54.00; 50.00              | 14.17                       | 14.00; 15.00; 13.50             | 770.33                      | 798.00; 823.00; 690.00          |
| FG1    | 51.00                        | 47.00; 54.00; 52.00              | 15.00                       | 16.00; 15.50; 15.00             | 857.27                      | 917.00; 846.10; 808.70          |
| FG2    | 52.17                        | 53.00; 50.50; 53.00              | 15.00                       | 16.00; 15.50; 15.00             | 775.33                      | 903.00; 727.00; 696.00          |
| FG3    | 51.00                        | 49.00; 54.00; 50.00              | 14.17                       | 14.00; 15.00; 13.50             | 770.33                      | 798.00; 823.00; 690.00          |
| FL1    | 51.00                        | 47.00; 54.00; 52.00              | 15.00                       | 16.00; 15.50; 15.00             | 857.27                      | 917.00; 846.10; 808.70          |
| FL2    | 52.17                        | 53.00; 50.50; 53.00              | 15.00                       | 16.00; 15.50; 15.00             | 775.33                      | 903.00; 727.00; 696.00          |
| FL3    | 51.00                        | 49.00; 54.00; 50.00              | 14.17                       | 14.00; 15.00; 13.50             | 770.33                      | 798.00; 823.00; 690.00          |
| FM1    | 51.00                        | 47.00; 54.00; 52.00              | 15.00                       | 16.00; 15.50; 15.00             | 857.27                      | 917.00; 846.10; 808.70          |
| FM2    | 52.17                        | 53.00; 50.50; 53.00              | 15.00                       | 16.00; 15.50; 15.00             | 775.33                      | 903.00; 727.00; 696.00          |
| FM3    | 51.00                        | 49.00; 54.00; 50.00              | 14.17                       | 14.00; 15.00; 13.50             | 770.33                      | 798.00; 823.00; 690.00          |
| MB1    | 31.33                        | 31.00; 32.00; 31.00              | 8.50                        | 8.00; 9.00; 8.50                 | 176.83                      | 169.00; 195.80; 165.70          |
| MB2    | 31.17                        | 31.00; 32.00; 30.50              | 8.83                        | 9.00; 8.50; 9.00                 | 159.73                      | 151.70; 161.30; 166.20          |
| MB3    | 30.67                        | 31.00; 30.50; 30.50              | 7.67                        | 8.00; 7.50; 7.50                 | 135.60                      | 138.20; 141.00; 127.60          |
| MG1    | 31.33                        | 31.00; 32.00; 31.00              | 8.50                        | 8.00; 9.00; 8.50                 | 176.83                      | 169.00; 195.80; 165.70          |
| MG2    | 31.17                        | 31.00; 32.00; 30.50              | 8.83                        | 9.00; 8.50; 9.00                 | 159.73                      | 151.70; 161.30; 166.20          |
| MG3    | 30.67                        | 31.00; 30.50; 30.50              | 7.67                        | 8.00; 7.50; 7.50                 | 135.60                      | 138.20; 141.00; 127.60          |
| ML1    | 31.33                        | 31.00; 32.00; 31.00              | 8.50                        | 8.00; 9.00; 8.50                 | 176.83                      | 169.00; 195.80; 165.70          |
| ML2    | 31.17                        | 31.00; 32.00; 30.50              | 8.83                        | 9.00; 8.50; 9.00                 | 159.73                      | 151.70; 161.30; 166.20          |
| ML3    | 30.67                        | 31.00; 30.50; 30.50              | 7.67                        | 8.00; 7.50; 7.50                 | 135.60                      | 138.20; 141.00; 127.60          |
| MM1    | 31.33                        | 31.00; 32.00; 31.00              | 8.50                        | 8.00; 9.00; 8.50                 | 176.83                      | 169.00; 195.80; 165.70          |
| MM2    | 31.17                        | 31.00; 32.00; 30.50              | 8.83                        | 9.00; 8.50; 9.00                 | 159.73                      | 151.70; 161.30; 166.20          |
| MM3    | 30.67                        | 31.00; 30.50; 30.50              | 7.67                        | 8.00; 7.50; 7.50                 | 135.60                      | 138.20; 141.00; 127.60          |
| PMB2   | 32.50                        | 33.00; 33.00; 31.50              | 8.00                        | 8.00; 8.00; 8.00                 | 167.47                      | 164.10; 175.80; 162.50          |
| PMB3   | 30.33                        | 28.00; 33.00; 30.00              | 7.83                        | 7.50; 8.00; 8.00                 | 167.87                      | 145.20; 169.60; 188.80          |
| Code   | CG   | CP   | CW   | CB   | CH   | CHH  | CCW  | CCW  | CCW  | CCW  |
|--------|------|------|------|------|------|------|------|------|------|------|
| PMG1   | 32.00| 31.00| 33.00| 32.00| 8.00 | 7.50 | 8.50 | 8.00 | 170.73| 145.30| 200.00| 166.90|
| PMG2   | 32.50| 33.00| 33.00| 31.50| 8.00 | 8.00 | 8.00 | 8.00 | 167.47| 164.10| 175.80| 162.50|
| PMG3   | 30.33| 28.00| 33.00| 30.00| 7.83 | 7.50 | 8.00 | 8.00 | 167.87| 145.20| 169.60| 188.80|
| PML1   | 32.00| 31.00| 33.00| 32.00| 8.00 | 7.50 | 8.50 | 8.00 | 170.73| 145.30| 200.00| 166.90|
| PML2   | 32.50| 33.00| 33.00| 31.50| 8.00 | 8.00 | 8.00 | 8.00 | 167.47| 164.10| 175.80| 162.50|
| PML3   | 30.33| 28.00| 33.00| 30.00| 7.83 | 7.50 | 8.00 | 8.00 | 167.87| 145.20| 169.60| 188.80|
| PMM1   | 32.00| 31.00| 33.00| 32.00| 8.00 | 7.50 | 8.50 | 8.00 | 170.73| 145.30| 200.00| 166.90|
| PMM2   | 32.50| 33.00| 33.00| 31.50| 8.00 | 8.00 | 8.00 | 8.00 | 167.47| 164.10| 175.80| 162.50|
| PMM3   | 30.33| 28.00| 33.00| 30.00| 7.83 | 7.50 | 8.00 | 8.00 | 167.87| 145.20| 169.60| 188.80|
| Tissue   | Gene ID    | Gene Symbol                                  | name      | primer sequences          |
|----------|------------|----------------------------------------------|-----------|---------------------------|
| brain    | 103396969  | growth arrest and DNA damage-inducible protein | gadd45g   | GCTGATGATGGTGAAAG         |
|          |            | GADD45 gamma                                 |           | AAATCCCTCAAAAAAGTA        |
| brain    | MSTRG.27059| Ubiquitin-conjugating enzyme E2L3             | ube2l3    | GAGGGTCTTTGACTGCTAT       |
| liver    | 103396100  | Cyclin Dependent Kinase 7                    | cdc7      | CTTTCAGTTTCAGTTACC        |
| (gonad)  |            |                                              |           | CATCACATTCTCTTTGCC        |
| liver    | 103386169  | cell death activator CIDE-3                  | cidec     | AAGAACAACCCCAAAGGAT       |
| gonad    | 103389623  | Origin recognition complex subunit 4         | orc4      | ATGTAGCAAGAGGAGGCC        |
| gonad    | 103397789  | proliferating cell nuclear antigen           | pcna      | GACTTTACCACACACAGC        |
| gonad    | 103390614  | minichromosome maintenance proteins 7        | mcm7      | GGGGTCGTCTCTACTTTGC       |
| gonad    | 103395116  | yorkie homolog                               | yap1      | TTAGACTGAATCTCTCTTTC      |
| gonad    | 103382170  | bone morphogenetic protein 2                 | bmp2      | GAGGAGCAGGAACACCA         |
| muscle   | 103397325  | Ubiquitin C                                  | ubc       | ATCTTCGCGACGACACT         |
| muscle   | 103382745  | Origin recognition complex subunit 5         | orc5      | AAGAAAAACGAAAGACG         |
| muscle   | 103389033  | cyclin B1                                    | ccnb1     | GACGCCATGGAGACAC         |
| all tissues | 103393304 | beta actin                                   | β-actin   | TACCTCCAGACAGCACAG       |
Table S5. The sequencing data information in the WGBS.

| Sample | Clean Reads Num | HQ Clean Reads Num(%) | Read Length | Adapter(%) | Low Quality(%) | N(%) | Mapped Ratio(%) | Sequence Depth |
|--------|-----------------|-----------------------|-------------|------------|---------------|------|----------------|----------------|
| FG1    | 111029356       | 110542962 (99.56%)    | 150/150     | 692 (0%)   | 485366 (0.44%) | 336 (0.0%) | 70.2           | 26.15          |
| FG2    | 112306940       | 111748082 (99.5%)     | 150/150     | 494 (0%)   | 557990 (0.5%)  | 374 (0.0%) | 69.91          | 26.32          |
| FG3    | 113117380       | 112596848 (99.51%)    | 150/150     | 588 (0%)   | 549566 (0.49%) | 378 (0.0%) | 70.39          | 26.7           |
| FM1    | 113706226       | 113209722 (99.56%)    | 150/150     | 566 (0%)   | 489316 (0.43%) | 6622 (0.01%) | 69.53          | 26.52          |
| FM2    | 112313732       | 111844468 (99.58%)    | 150/150     | 700 (0%)  | 462766 (0.41%) | 5798 (0.01%) | 70.34          | 26.51          |
| FM3    | 110305108       | 109727720 (99.48%)    | 150/150     | 476 (0%)   | 576504 (0.52%) | 408 (0.0%) | 70.14          | 25.93          |
| MG1    | 110480040       | 110020972 (99.58%)    | 150/150     | 550 (0%)   | 458118 (0.41%) | 400 (0.0%) | 71.28          | 26.43          |
| MG2    | 109414182       | 109035938 (99.65%)    | 150/150     | 410 (0%)   | 371380 (0.34%) | 6454 (0.01%) | 71.78          | 26.37          |
| MG3    | 106360760       | 105945058 (99.61%)    | 150/150     | 484 (0%)   | 409094 (0.38%) | 6124 (0.01%) | 71.06          | 25.37          |
| MM1    | 107172150       | 106750238 (99.61%)    | 150/150     | 542 (0%)   | 415064 (0.39%) | 6306 (0.01%) | 70.67          | 25.42          |
| MM2    | 154243232       | 153305570 (99.39%)    | 150/150     | 1330 (0%)  | 935892 (0.61%) | 440 (0.0%) | 69.39          | 35.85          |
| MM3    | 115589994       | 115113764 (99.59%)    | 150/150     | 624 (0%)   | 468978 (0.41%) | 6628 (0.01%) | 70.75          | 27.44          |
| PMG1   | 156672578       | 155868440 (99.49%)    | 150/150     | 1326 (0%)  | 802374 (0.51%) | 438 (0.0%) | 70.25          | 36.9           |
| PMG2   | 109047052       | 108503390 (99.5%)     | 150/150     | 520 (0%)   | 542820 (0.5%)  | 322 (0.0%) | 70.43          | 25.75          |
| PMG3   | 1164777536      | 116040944 (99.54%)    | 150/150     | 434 (0%)   | 535750 (0.46%) | 408 (0.0%) | 70.63          | 27.6           |
| PMM1   | 109496918       | 108933954 (99.49%)    | 150/150     | 508 (0%)   | 562082 (0.51%) | 374 (0.0%) | 69.79          | 25.62          |
| PMM2   | 110362622       | 109618918 (99.33%)    | 150/150     | 1176 (0%)  | 736050 (0.67%) | 6478 (0.01%) | 69.13          | 25.53          |
| PMM3   | 112593252       | 111843020 (99.33%)    | 150/150     | 1498 (0%)  | 742150 (0.66%) | 6584 (0.01%) | 68.98          | 26.0           |
Table S6. The genomic DNA methylation levels in 18 samples.

| Sample | C(%)  | CG(%) | CHG(%) | CHH(%) |
|--------|-------|-------|--------|--------|
| FG1    | 7.27  | 65.48 | 0.74   | 0.78   |
| FG2    | 7.27  | 66.02 | 0.68   | 0.71   |
| FG3    | 7.31  | 66.5  | 0.68   | 0.71   |
| FM1    | 7.29  | 65.87 | 0.68   | 0.75   |
| FM2    | 7.27  | 65.88 | 0.68   | 0.74   |
| FM3    | 7.24  | 65.39 | 0.7    | 0.77   |
| MG1    | 8.55  | 80.99 | 0.45   | 0.47   |
| MG2    | 8.48  | 80.5  | 0.46   | 0.48   |
| MG3    | 8.78  | 80.89 | 0.69   | 0.72   |
| MM1    | 7.42  | 67.34 | 0.68   | 0.73   |
| MM2    | 7.27  | 68.1  | 0.46   | 0.51   |
| MM3    | 7.59  | 68.69 | 0.72   | 0.77   |
| PMG1   | 8.67  | 80.28 | 0.65   | 0.68   |
| PMG2   | 8.87  | 81.53 | 0.73   | 0.75   |
| PMG3   | 8.8   | 81    | 0.71   | 0.74   |
| PMM1   | 7.8   | 71.25 | 0.71   | 0.76   |
| PMM2   | 7.4   | 67.14 | 0.73   | 0.79   |
| PMM3   | 7.68  | 69.98 | 0.73   | 0.79   |