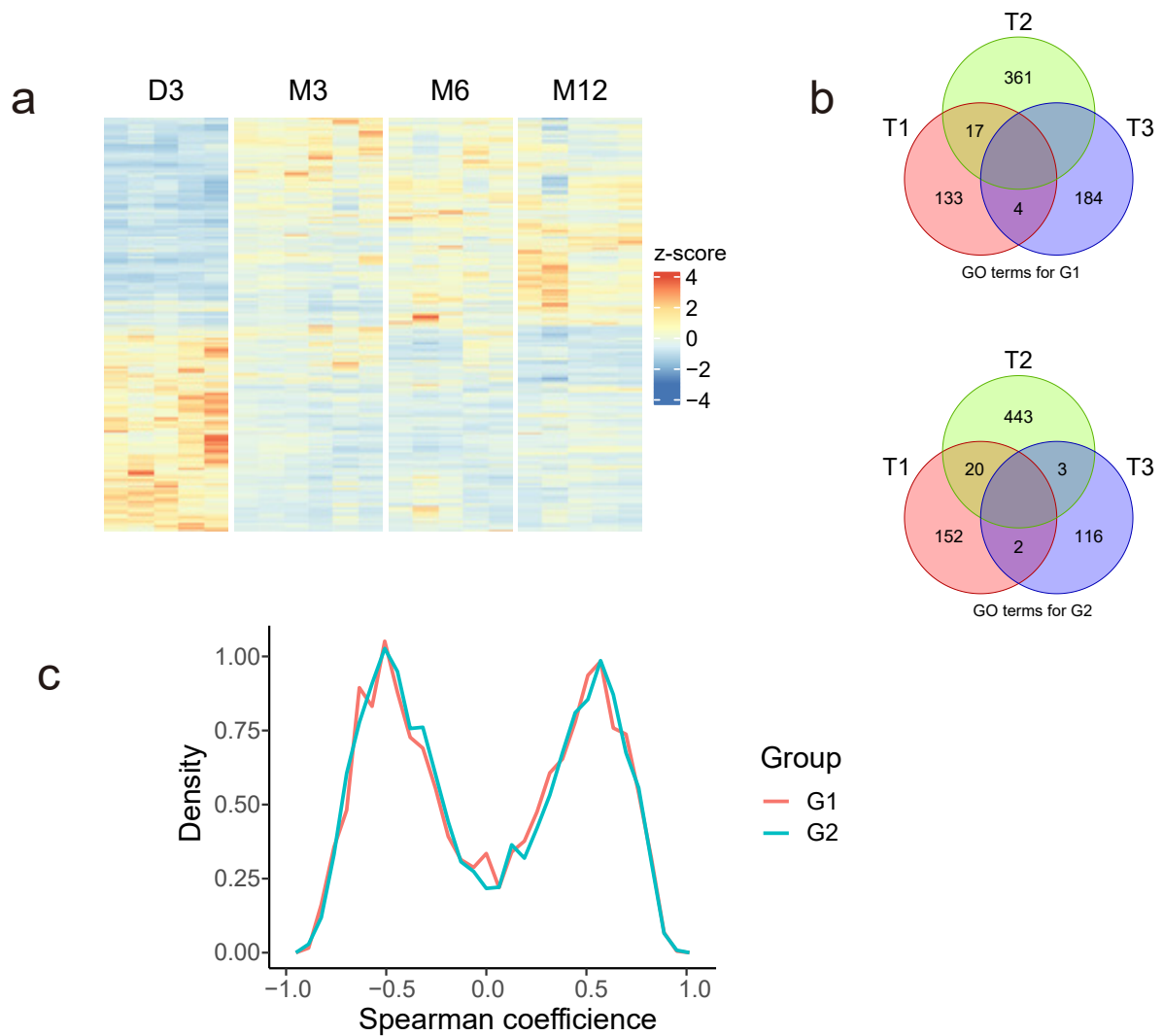


Supplementary Table 1

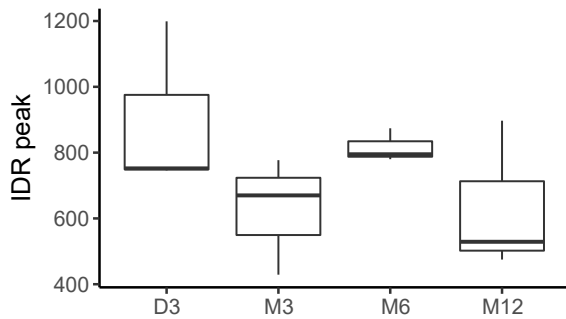
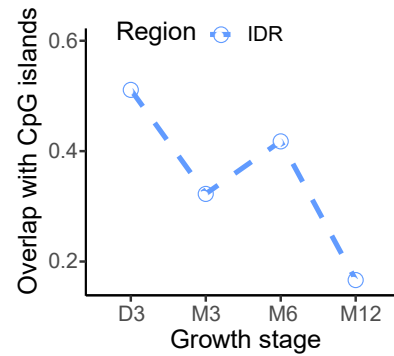
Key resources table

RESOURCE	SOURCE	IDENTIFIER
Deposited data		
Sheep reference genome Oar_v4.0 (Oar_v4.0)	NCBI	https://www.ncbi.nlm.nih.gov/assembly/GCF_000298735.2
WGS (whole genome sequence) data	NCBI SRA	SRR10821772, SRR11657579-SRR11657583
ChIP-seq data (H3K4me3)	NCBI SRA	SRR5070525-SRR5070530
ChIP-seq data (H3K27ac)	NCBI SRA	SRR5070519-SRR5070524
ChIP-seq data (nucleosomal DNA)	NCBI SRA	SRR5070531
TF database hTFtarget	Zhang,Q. et al, 2020	http://bioinfo.life.hust.edu.cn/hTFtarget#!/download
Software and algorithms		
Trim_galore 0.6.6	the Babraham Institute	https://www.bioinformatics.babraham.ac.uk/projects/trim_galore/
Hisat2 2.2.1	Danecek, Petr et al., 2019	http://daehwankimlab.github.io/hisat2/
Samtools 1.9	Danecek, Petr et al., 2021	https://www.htslib.org/
featureCounts subread 2.0.1	Liao Y, Smyth GK and Shi W., 2014	http://subread.sourceforge.net/
DESeq2 1.26.0	Love, Michael I., Wolfgang Huber, and Simon Anders. 2014	https://bioconductor.org/packages/release/bioc/html/DESeq2.html
Bowtie2 2.35.1	Langmead and Salzberg, 2012	https://github.com/BenLangmead/bowtie2
Samamba 0.6.6	Artem Tarasov et al.,2015	https://github.com/biod/sambamba
MACS2 2.1.0	Zhang, Y., Liu, T., Meyer, C.A. et al., 2008	https://github.com/macs3-project/MACS
BEDTools 2.29.2	the Quinlan laboratory at the University of Utah	https://bedtools.readthedocs.io/en/latest/index.html
Bismark 0.23.0	the Babraham Institute	https://github.com/FelixKrueger/Bismark
GATK4 4.1.8	the Broad Institute	https://gatk.broadinstitute.org/hc/en-us
Biscuit 0.3.16	the Van Andel Institute	https://huishenlab.github.io/biscuit/

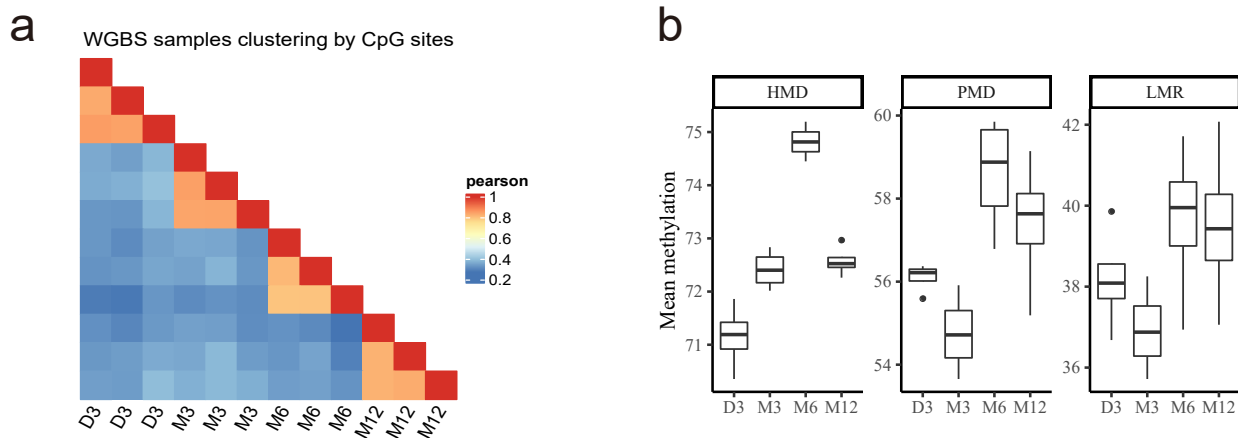
ClusterProfiler 3.14.3	G Yu, et al., 2008	https://bioconductor.org/packages/release/bioc/html/clusterProfiler.html
ChIPseeker 1.26.2	G Yu, et al., 2015	https://bioconductor.org/packages/release/bioc/html/ChIPseeker.html
Kohonen 3.0.10	Wehrens R, Kruisselbrink J, 2018	https://cran.r-project.org/web/packages/kohonen/index.html
Mfuzz 2.46.0	Matthias E. Futachik and Bronwyn Carlisle, 2005	http://mfuzz.sysbiolab.eu/
MethylSeekR 1.26.0	Lukas Burger, et al, 2013	https://bioconductor.riken.jp/packages/3.10/bioc/html/MethylSeekR.html
DiffBind 2.14.0	Cancer Research UK's Cambridge Research Institute	https://bioconductor.riken.jp/packages/release/bioc/html/DiffBind.html
DSS 2.38.0	Feng, Conneely, and Wu (2014)	https://bioconductor.riken.jp/packages/release/bioc/html/DSS.html
HOMER	Christopher Benner, University of California, San Diego	http://homer.ucsd.edu/homer/motif/
pyGenomeTracks 3.6	Fidel Ramírez, et al, 2018	https://github.com/deeptools/pyGenomeTracks
IDR 2.0.4.2	Li, Brown, Huang, and Bickel, 2011	https://github.com/kundajelab/idr



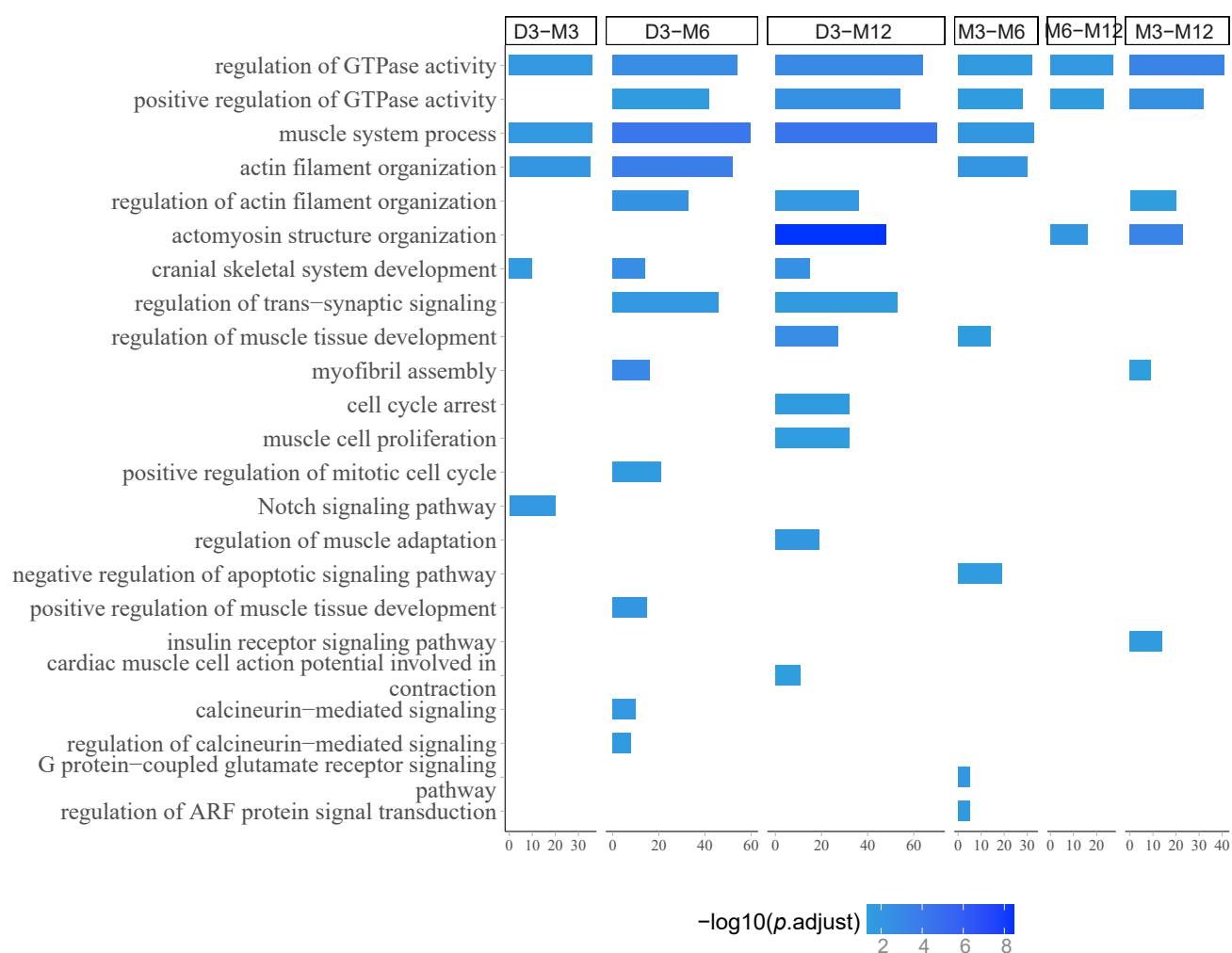
Supplementary Figure 1. **Difference among DEG groups base on expression cluster results** (a) Expression heatmap of DEG across four stages. (b) Venn diagram of GO terms of three tendencies (T1-T3) for G1 and G2 group, respectively. (c) Distribution of spearman correlation coefficient for G1(red line) and G2 groups (blue line). DEG: differntial expressed genes; GO: gene ontology.

a**b**

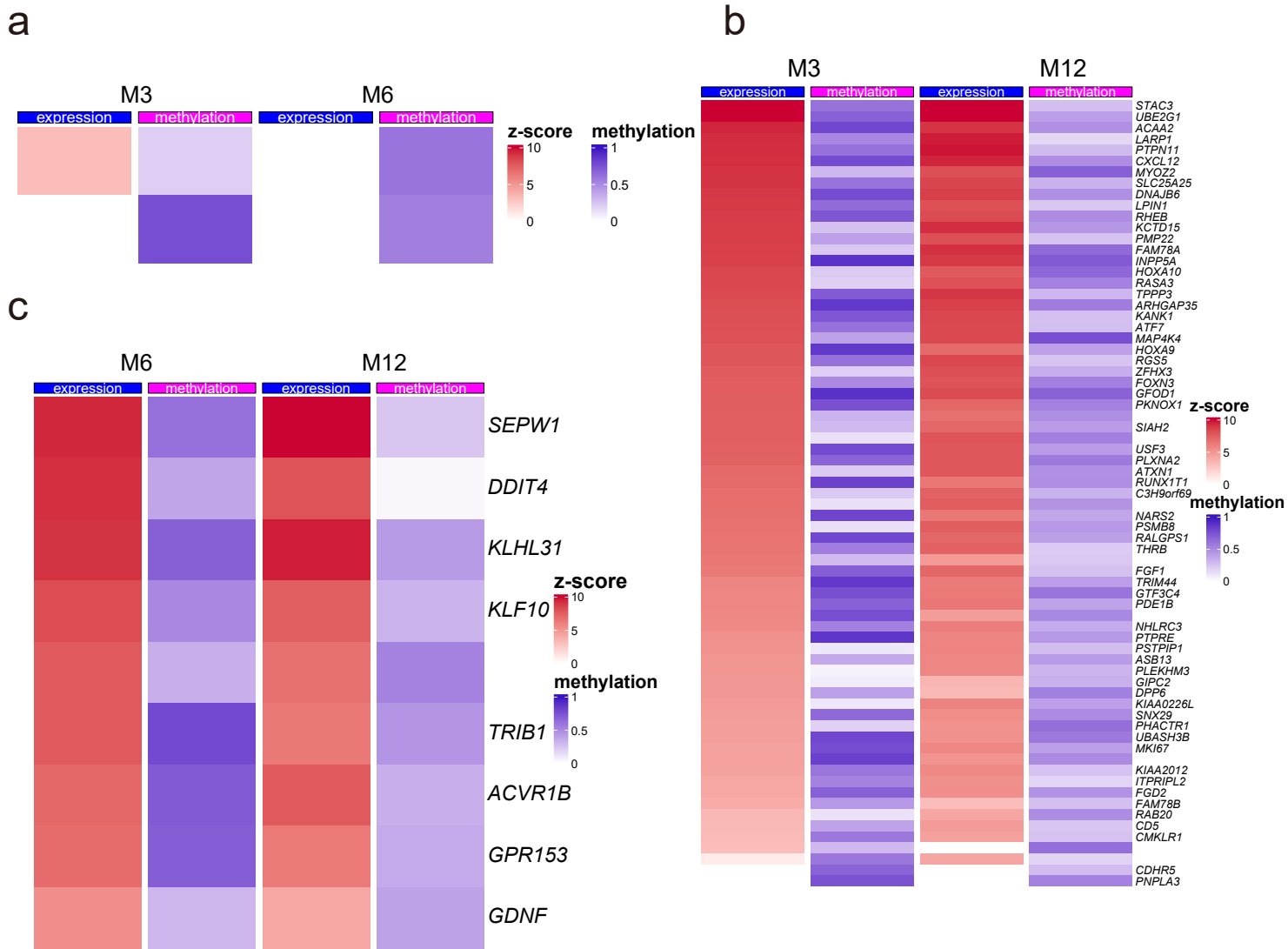
Supplementary Figure 2. **IDR peaks and its proportion overlapped with CpG islands** (a) Box plot summarizing number of IDR peaks across four stages. Boxes represent 25th to 75th percentile and whiskers represent minimum-maximum. Horizontal lines within boxes represent the median. (b) Line plot exhibiting number of IDR peaks located on CpG islands across four stages. IDR: irreproducibility discovery rate.



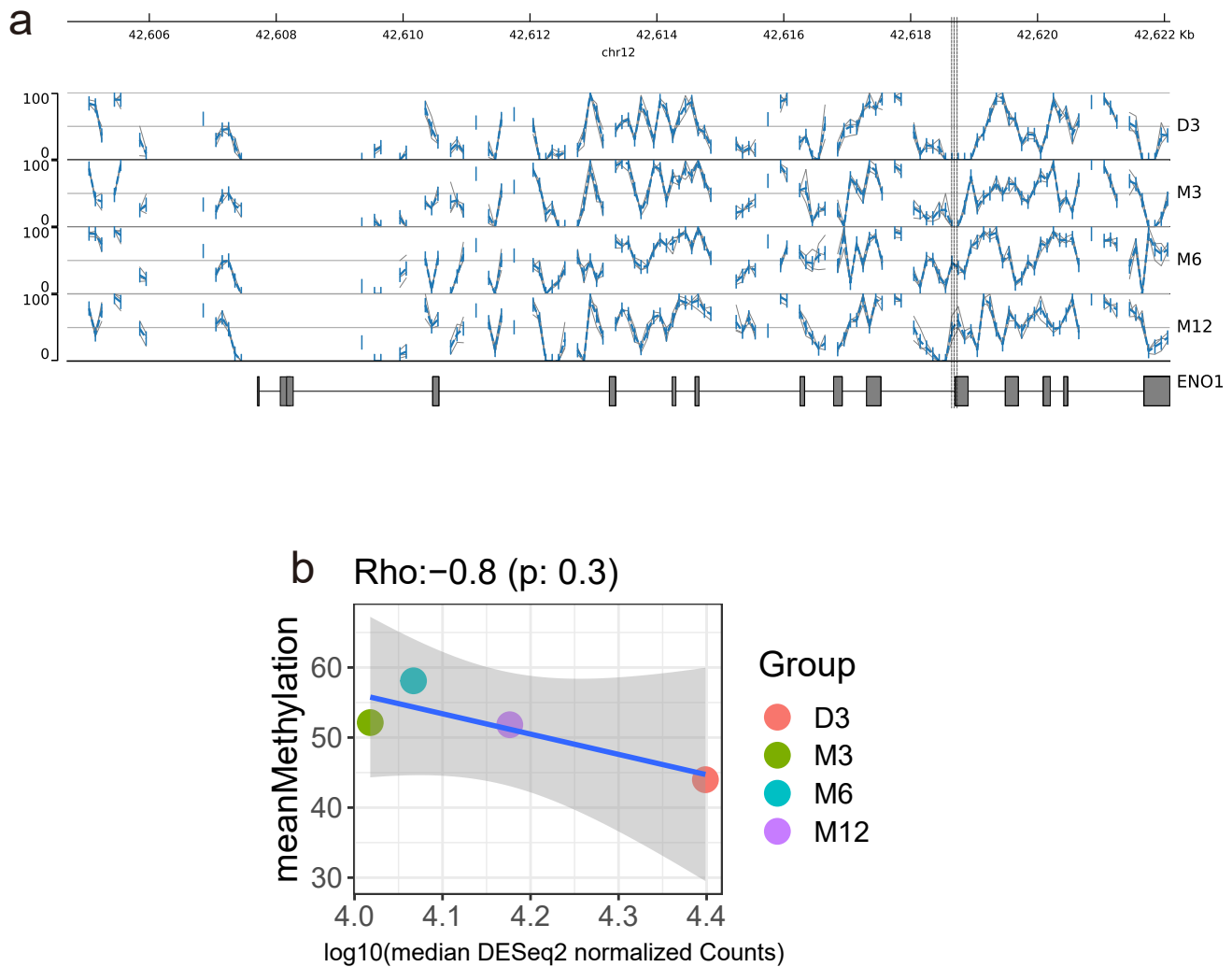
Supplementary Figure 3. **Overview of sample correlation based on methylation and methylation type.** (a) Heatmap of Pearson's correlation coefficient based on methylations of CpG sites. (b) Box plot summarizing mean methylation of HMD, PMD and LMR across four stages. Boxes represent 25th to 75th percentile and whiskers represent minimum-maximum. Horizontal lines within boxes represent the median. HMD: high methylated domains; PMD: partially methylated domains; LMR: low methylated regions.



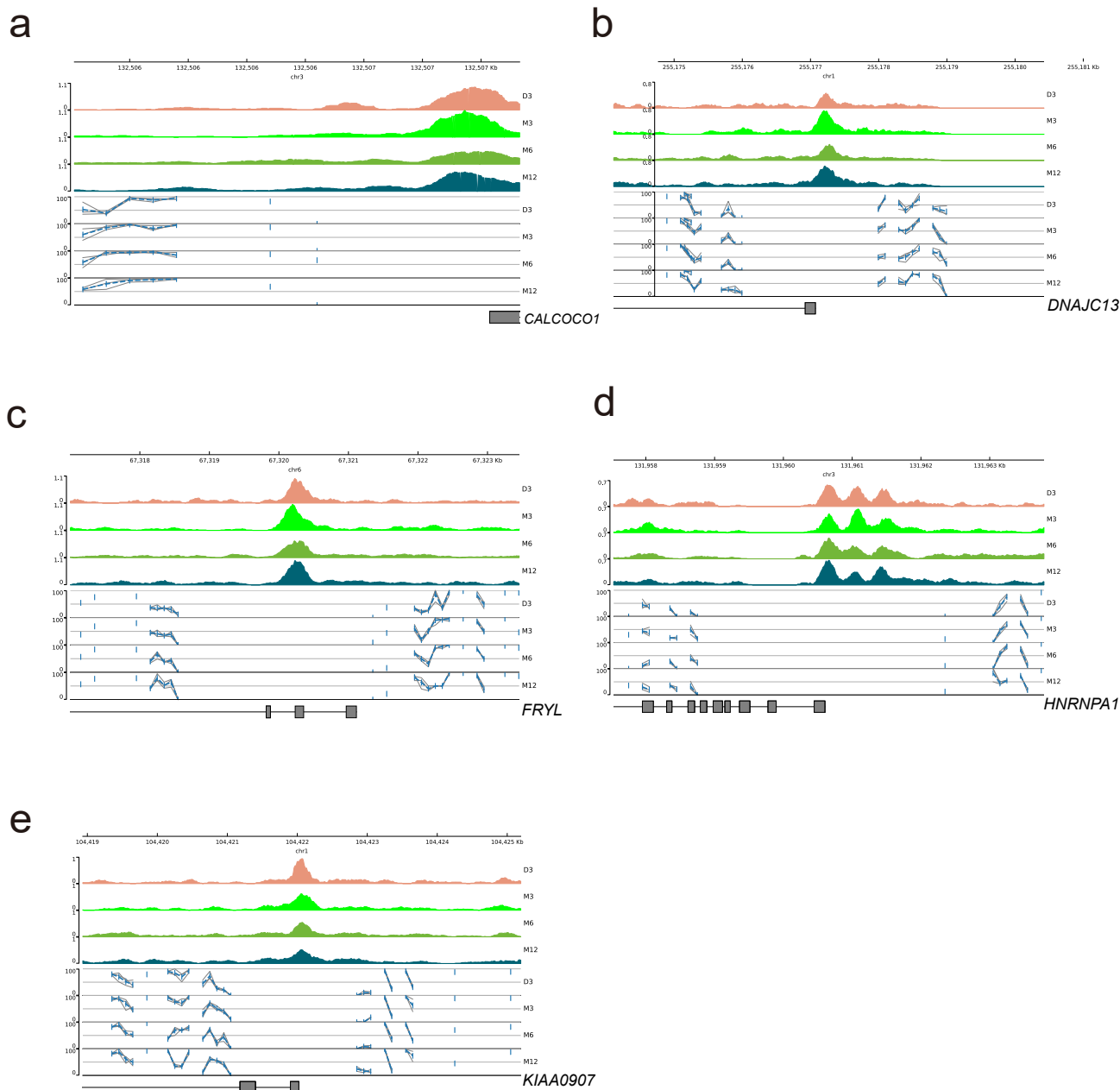
Supplementary Figure 4. **Overview of functional annotations of DMR.** GO items of DMR for all six comparison groups. DMR: differentially methylated regions. GO: gene ontology



Supplementary Figure 5. **Methylation and transcription profile of DEG with DMR annotations.** Heatmap for gene expression (red -blue bar, red indicates high expression while blue means low expression) and their methylation at DMR (purple bar, the deeper purple, the higher DNA methylation) for M3-M6 (a), M3-M12 (b) and M6-M12 (c). DEG: differentially expressed genes; DMR: differentially methylated regions.



Supplementary Figure 6. **Methylation of *ENO1* and its correlation with transcription levels and methylation type.** (a) The methylation level on whole sequence was displayed and the dashed line indicated where the DMR is. GCF_000298735.2 was used for genome annotation. (b) The dot plot displayed the relationship between mean methylation on the *ENO1*'s body region and median expression of *ENO1*. Shading area indicated the 95% confidence interval. The spearman correlation (ρ) was -0.8 , while the p -value is 0.3 . DMR: differentially methylated regions.



Supplementary Figure 7. **Candidate genes subjected to the interaction effect of accessible chromosome and methylation regions.** Genome browser of chromosome accessibility and DNA methylation on promoter for *CALCOCO1* (a), *DNAJC13* (b), *FRYL* (c), *HNRNPA1* (d) and *KIAA0907* (e). GCF_000298735.2 was used for genome annotation.