

Comprehensive multi-tissue epigenome atlas in sheep: A resource for complex traits, domestication and breeding

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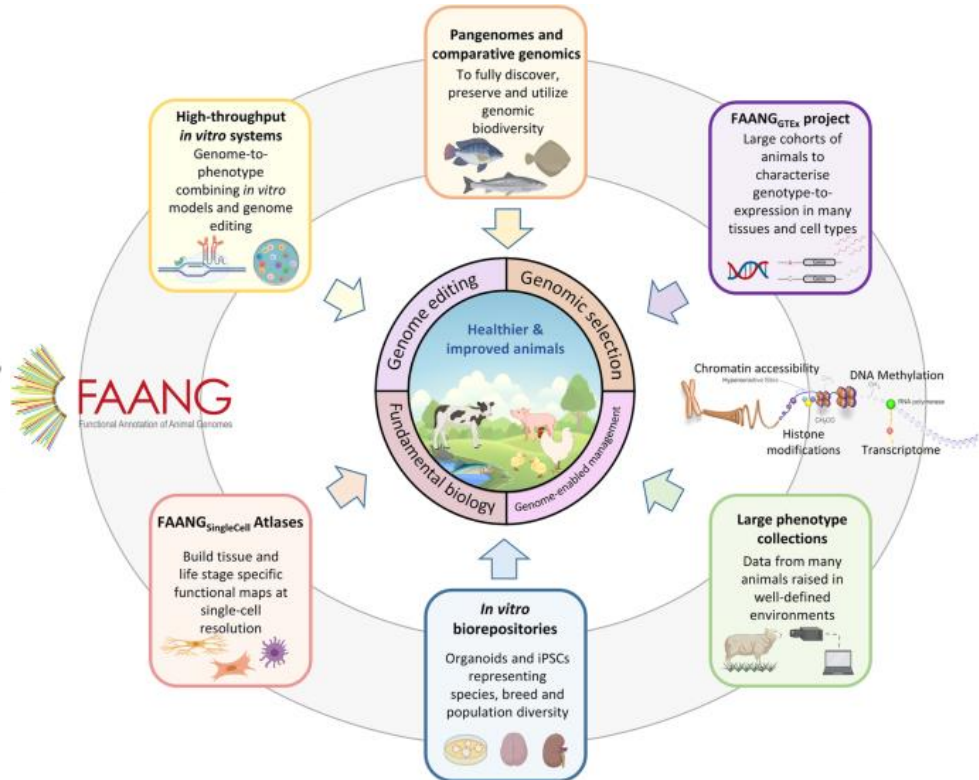
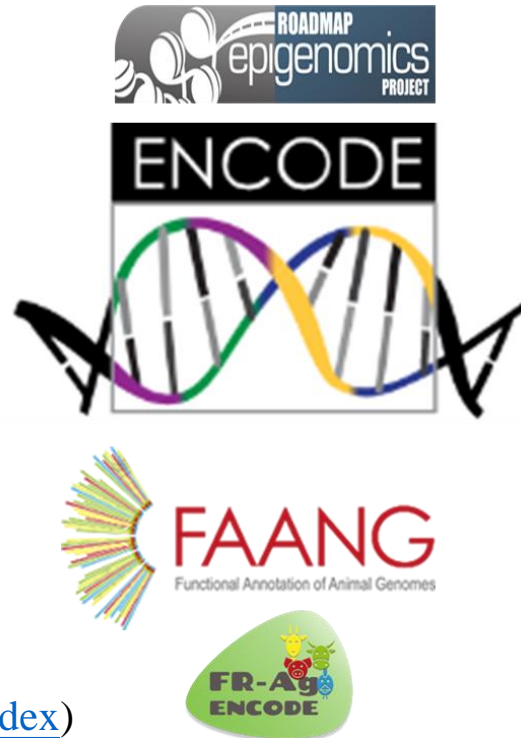
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Introduction



Sheep QTLs data

(<https://www.animalgenome.org/cgi-bin/QTLdb/index>)



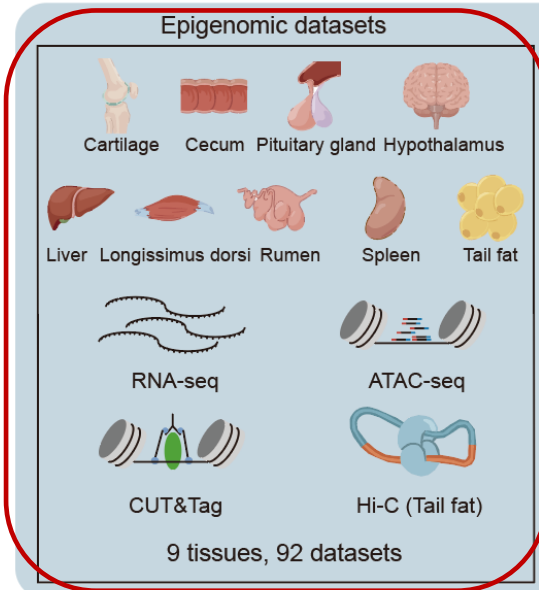
(Clark EL et al., 2020, Genome Biol)

- Most of the functional sites are located in non-coding regions of the genome;
- The annotation of functional elements in the sheep genome is still limited.

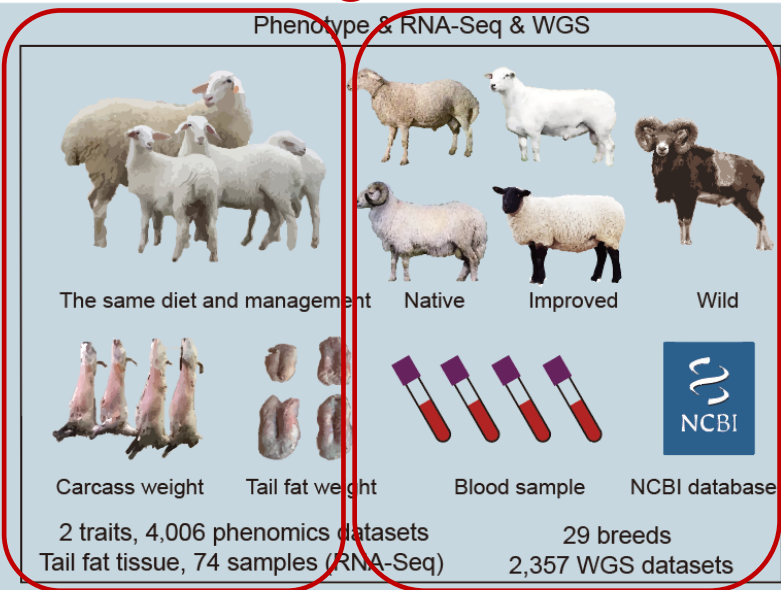


Highlights

① Data generation

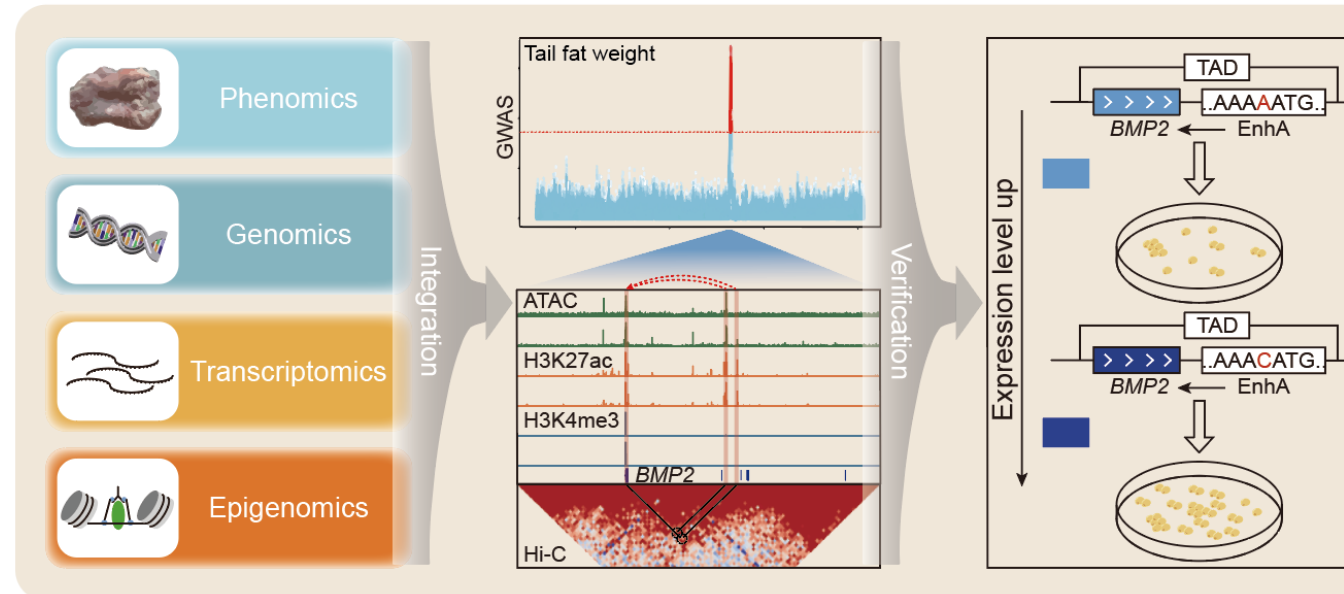


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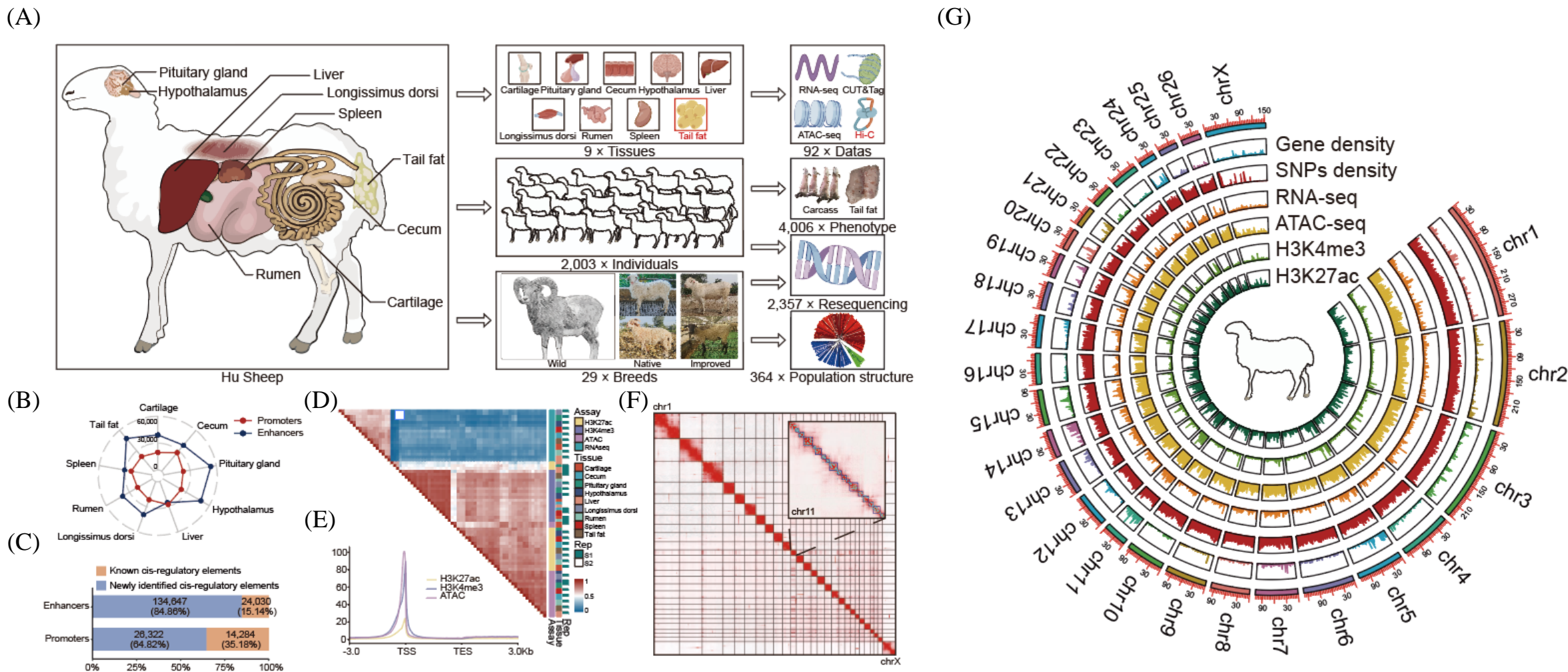


③

Bioinformatics analysis



Overview of sheep multi-tissue epigenomic atlas



(A) Schematic overview of the organization and dataset;
 (B-E) Annotation of functional regulatory elements; (F) 3D genome interaction map.

(G) Circos plot summarizing the chromosomal distribution of epigenetic marks.

Figure 1. Multi-tissue sheep epigenome atlas

Definition and characterization of chromatin states

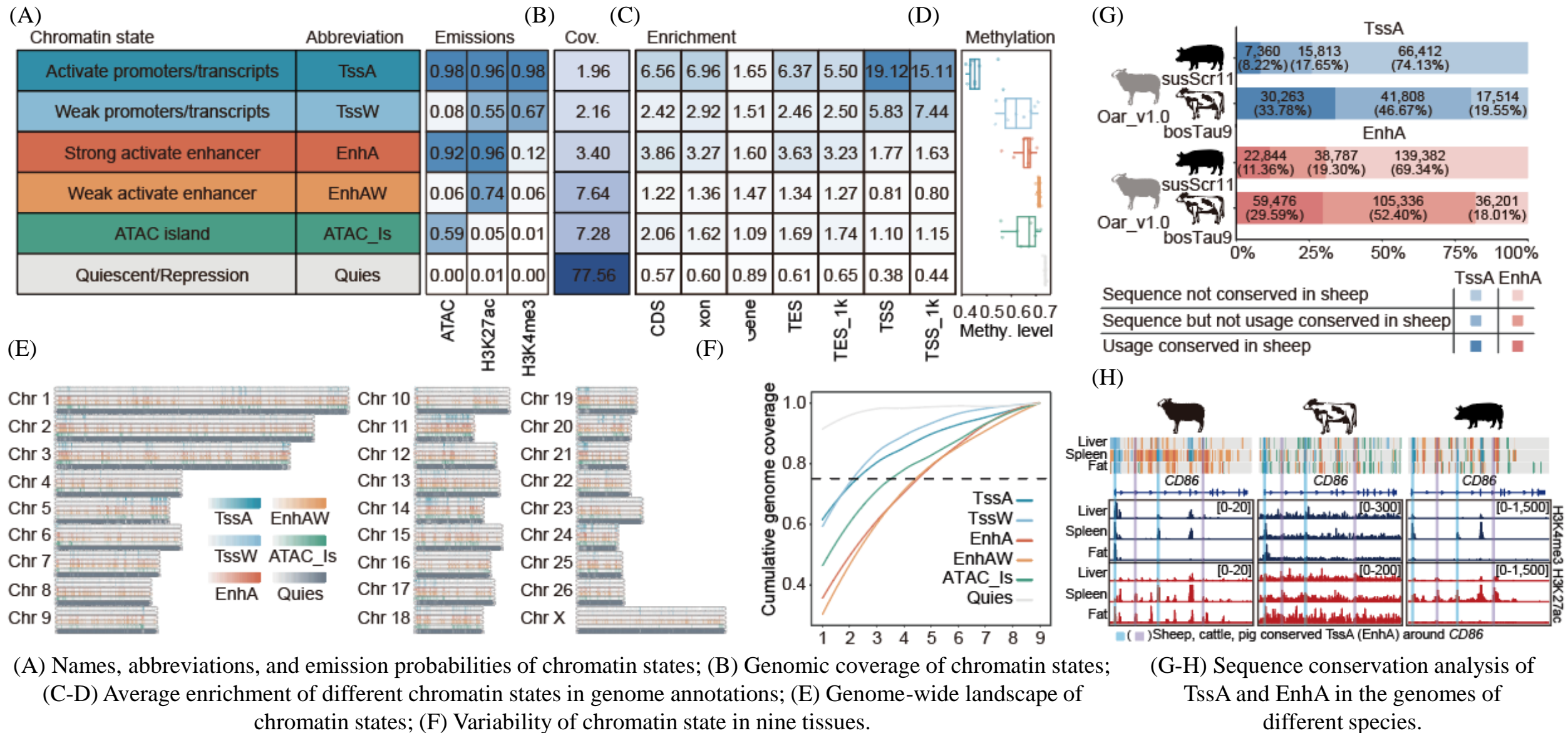
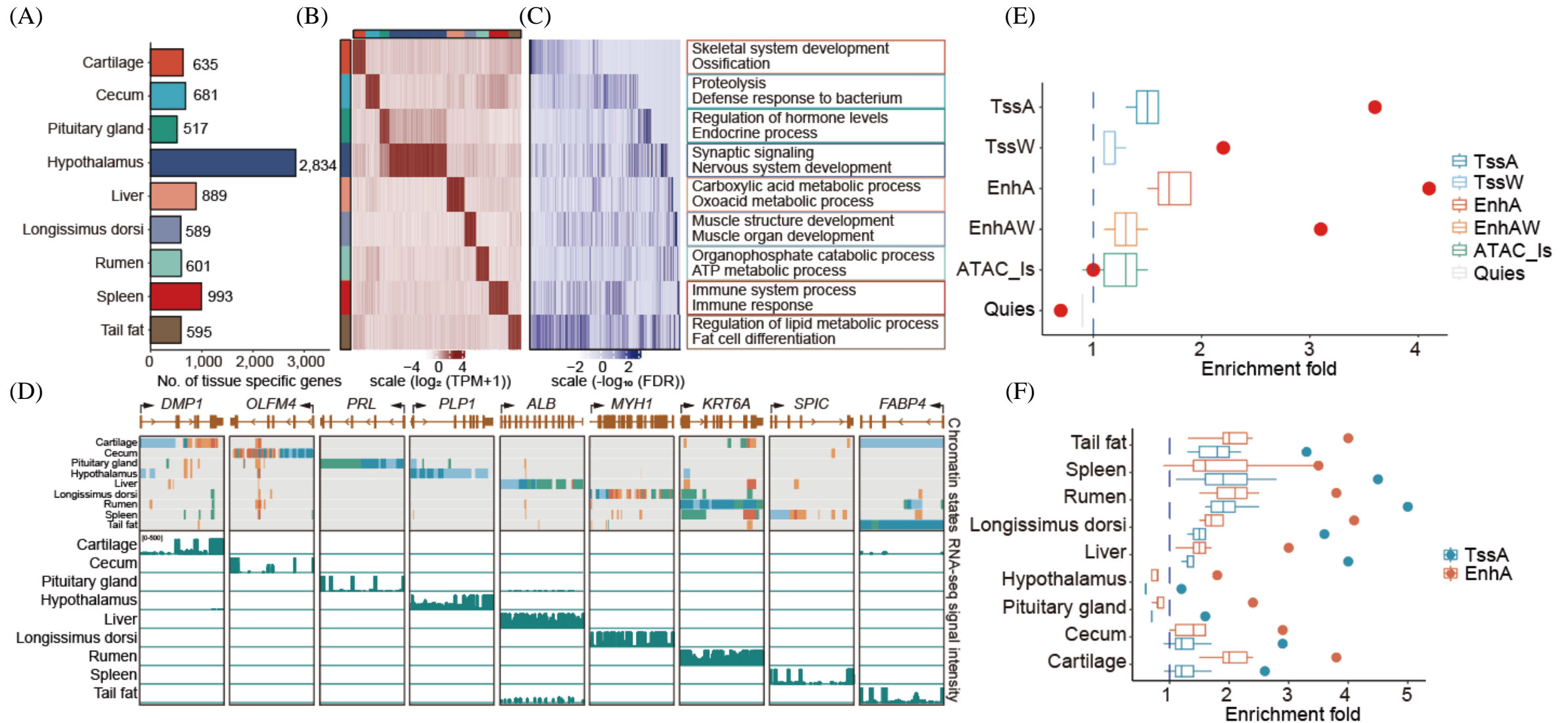


Figure 2. Prediction of chromatin states and species conservation analysis

Tissue-specific analysis of gene and chromatin states

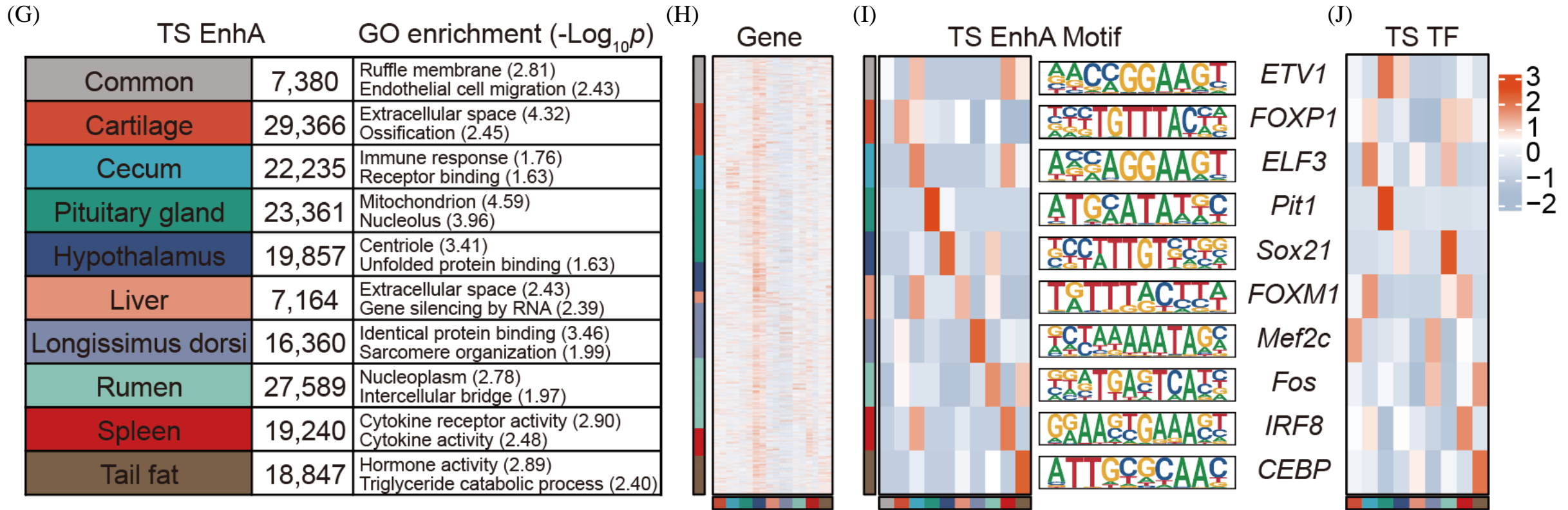


(A) Number of tissue-specific genes; (B) Expression pattern; (C) GO enrichment;
(D) Chromatin state pattern of tissue-specific genes.

(E-F) Enrichment patterns of chromatin states in tissue-specific genes.

Figure 3. Functional characterization of tissue-specific genes and chromatin states

Tissue-specific analysis of gene and chromatin states



(G) Number of tissue-specific enhancers and GO functional enrichment of target genes; (H) Expression pattern of target genes; (I) Motifs enriched in tissue-specific enhancers; (J) Expression levels of motif-binding transcription factors.

Figure 3. Functional characterization of tissue-specific genes and chromatin states



Chromatin state predictions that enhance the understanding of phenotypic variation

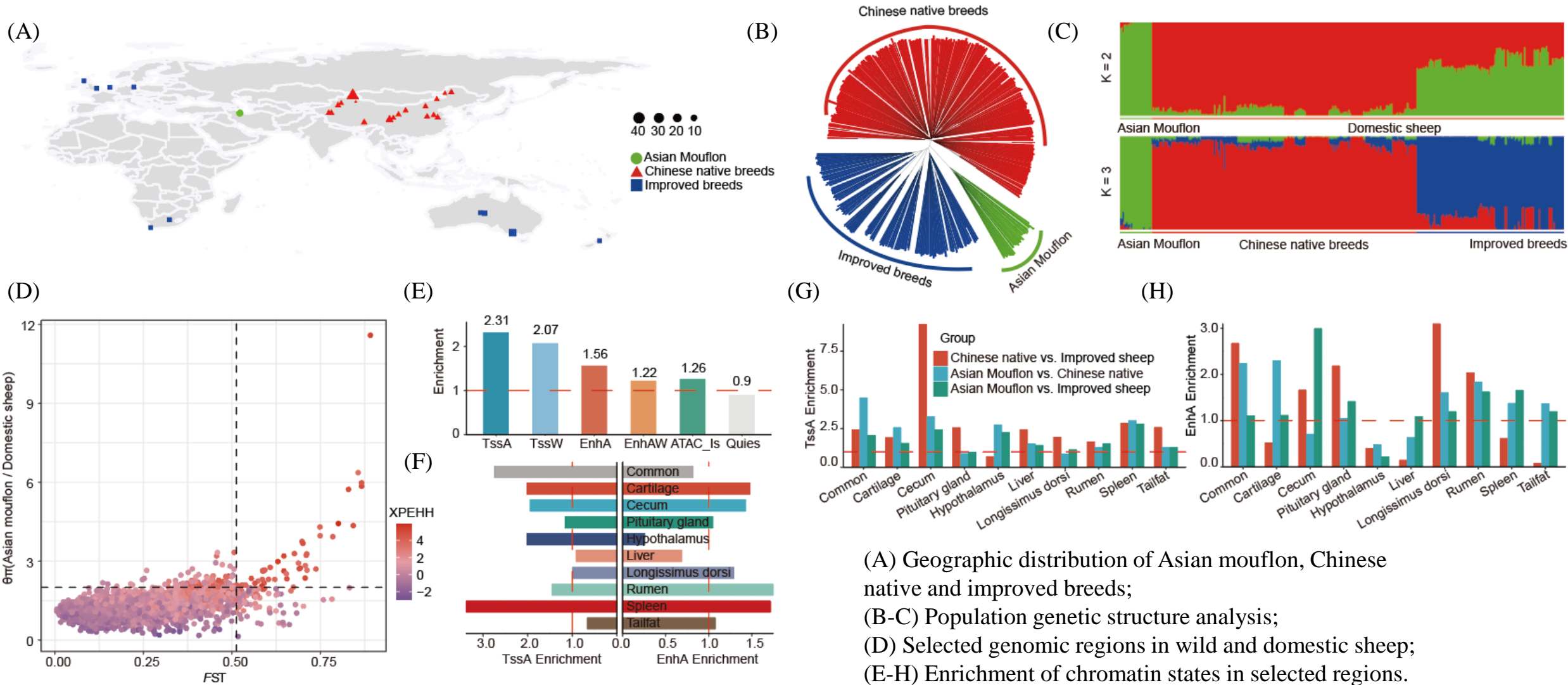


Figure 4. Enrichment of chromatin status for selected regions during sheep domestication and improvement

Genome-wide selection analysis of sheep with distinct tail morphology

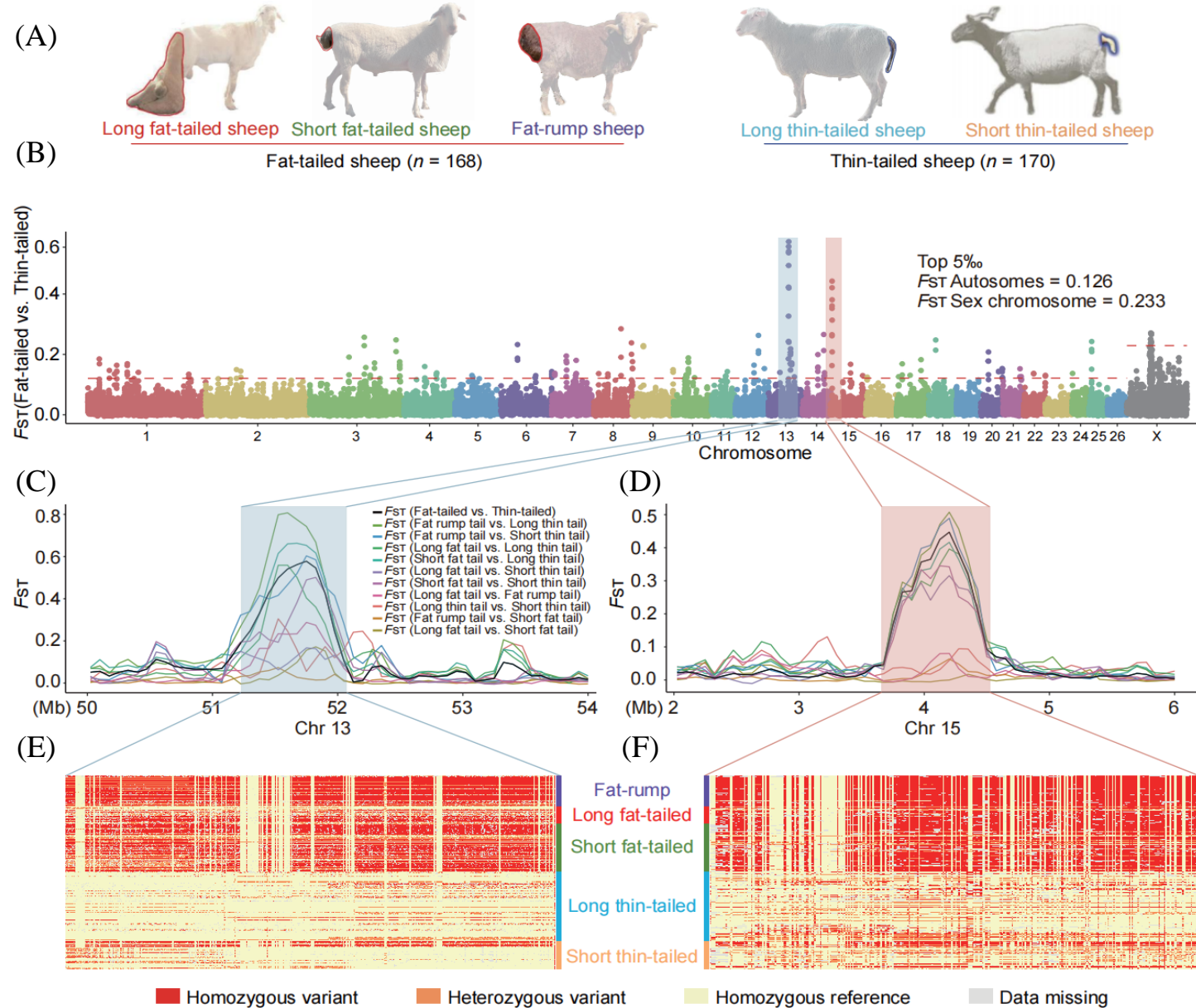
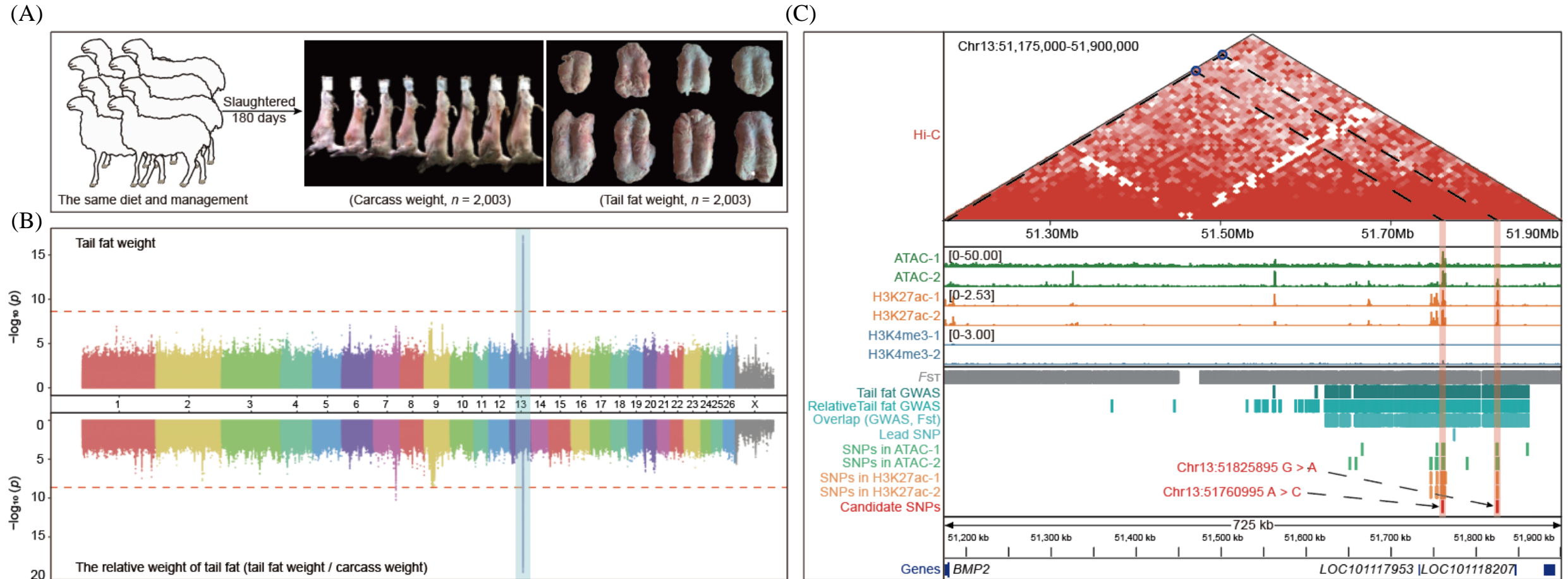


Figure 5. Genome-wide selection sweep test of sheep with distinct tail morphology



Integrating GWAS and epigenomes data

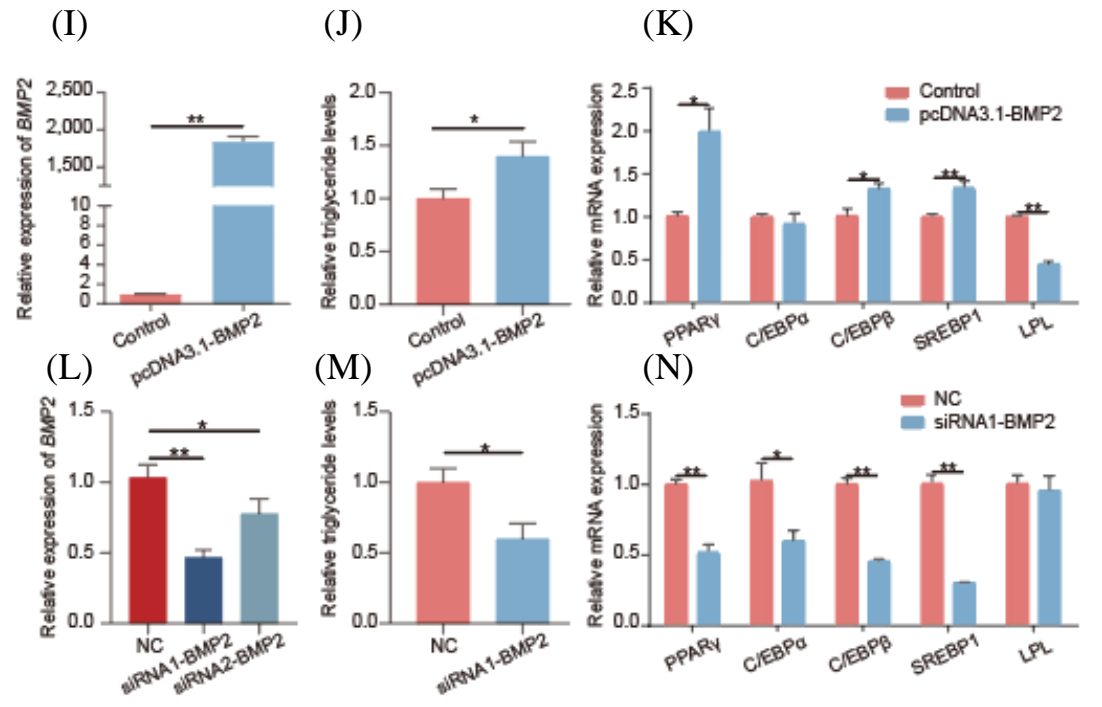
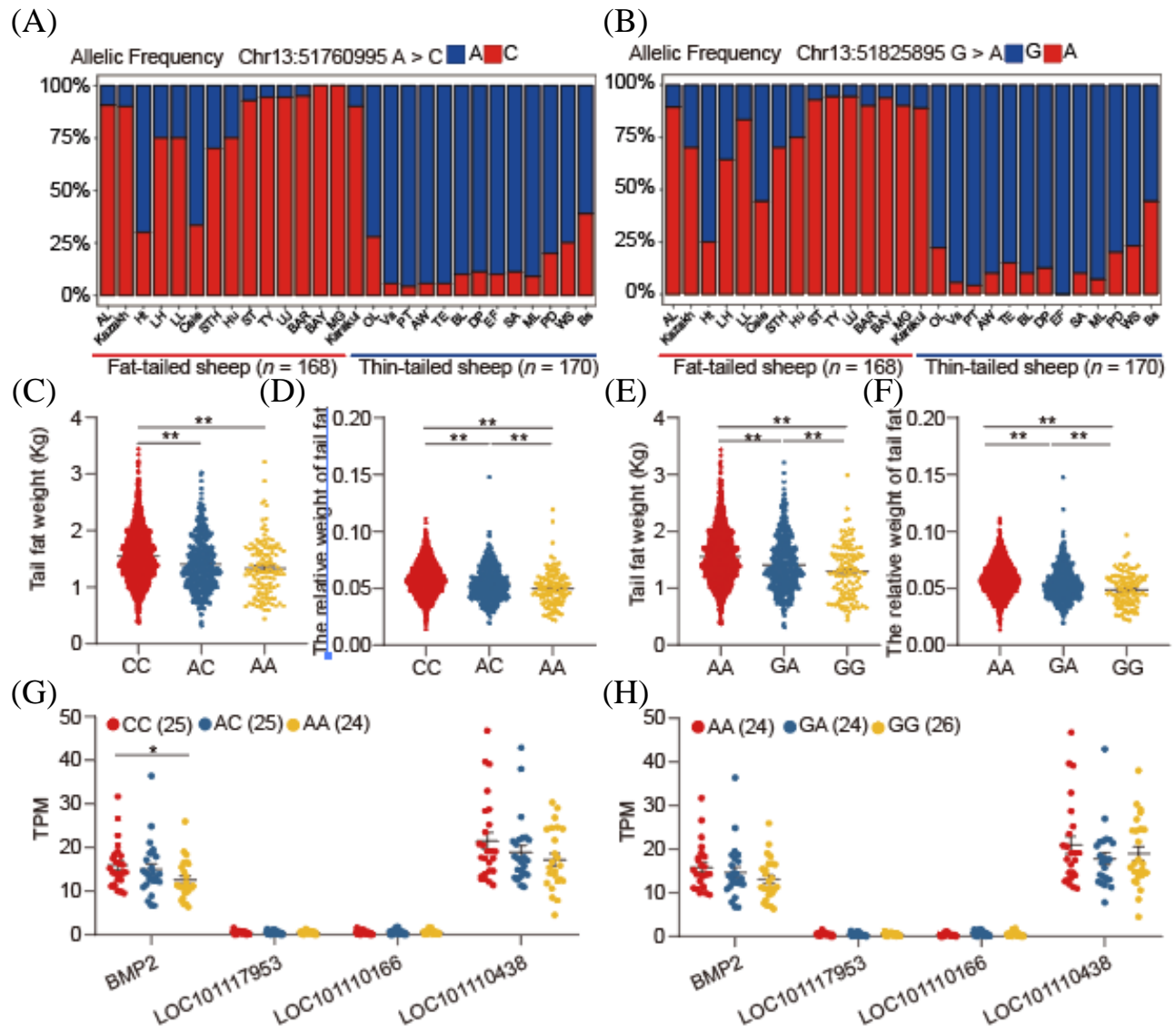


(A) Schematic diagram of tail fat-related trait determination;
(B) GWAS of tail fat weight and tail fat relative weight (tail fat weight/carcass weight) of Hu sheep;
(C) Integrated analysis of genomic and epigenomic data (ATAC-seq, CUT&Tag, Hi-C).

Figure 6. Integrative analysis of multiple omics datasets



Identification of causal variant and verification of target genes



(A-B) Allele frequency distribution of candidate loci in sheep breeds with different tail types;
 (C-F) Tail fat weight and relative tail fat weight of different genotypes of Chr13:51760995A>C and Chr13:51825895G>A;
 (G-H) Expression levels of candidate genes in different genotypes of Chr13:51760995A>C and Chr13:51825895G>A;
 (I-N) Experimental verification of target gene *BMP2*.

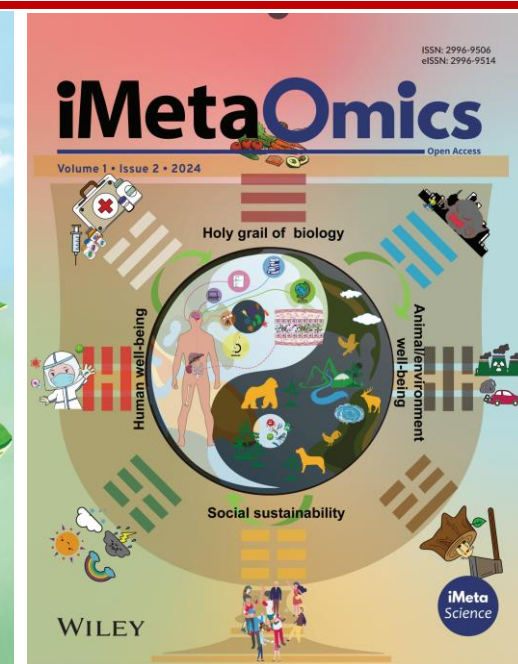
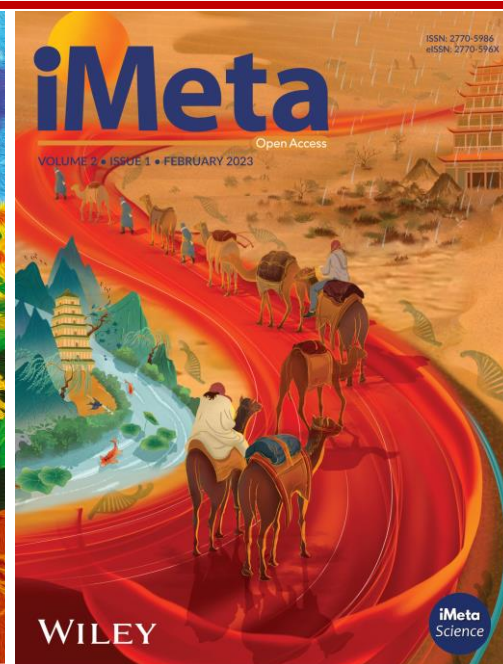
Figure 7. Identification of causal variant and verification of target genes



Summary



- ❑ In this study, we established the first multi-tissue epigenomic blueprint of sheep to fill a knowledge gap in existing sheep atlas datasets;
- ❑ This atlas provides foundational data resources for understanding the adaptive evolution and complex economic traits of sheep;
- ❑ Through integration analysis of our multi-layered datasets, we identified a novel causal SNP (Chr13:51760995 A > C) that could serve as potential genetic marker for reducing tail fat deposition in sheep breeding programs;
- ❑ Overall, these findings provide valuable resources and molecular marker applicable to sheep breeding, helping to accelerate genetic improvement.


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