

Supplementary information, Figure S1

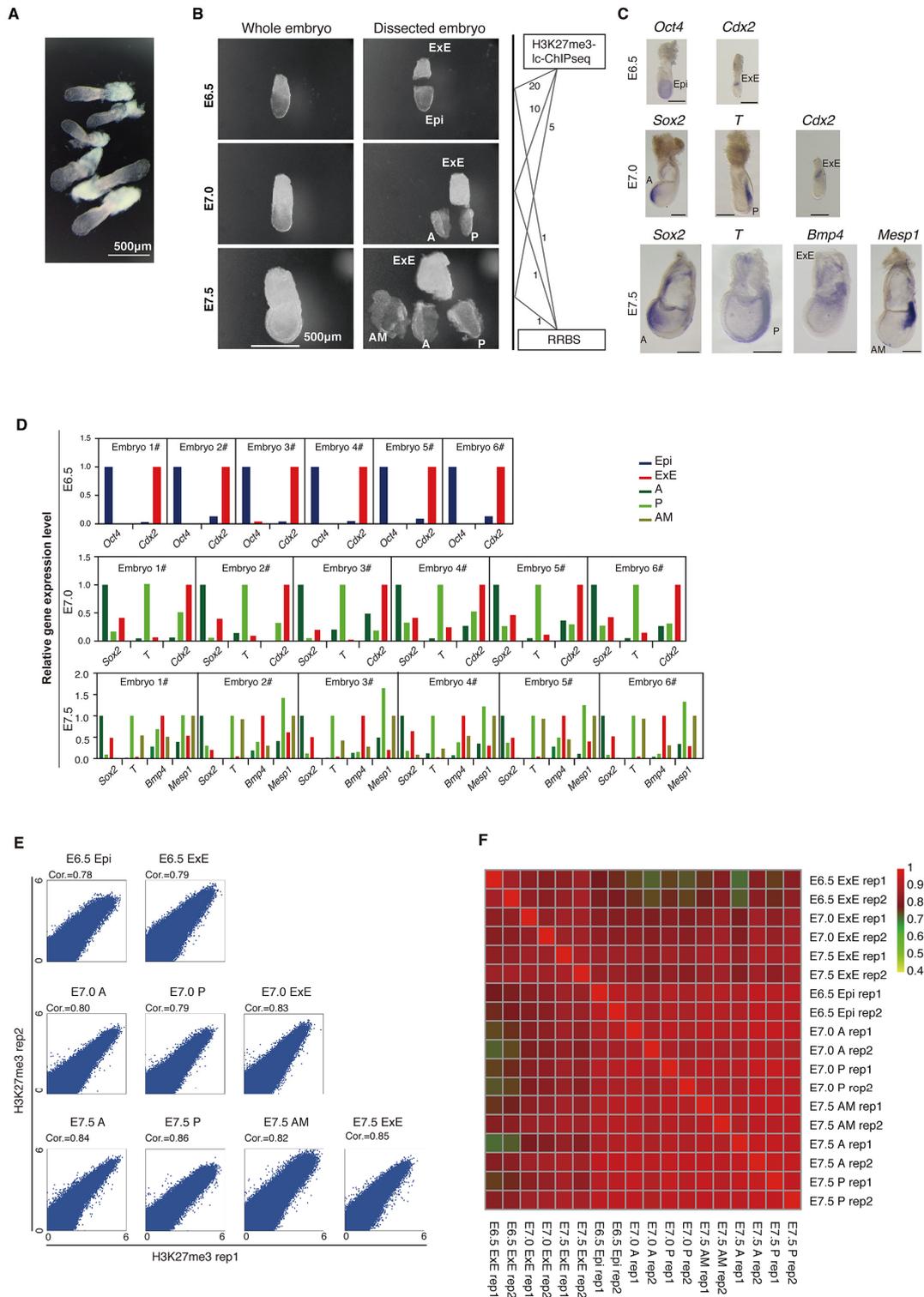


Figure S1 Epigenetic profiling of the mouse post-implantation embryos. **(A)** The morphology of the mouse gastrula. **(B)** Manipulation strategy of the mouse embryos

from E6.5 to E7.5 stage. The numbers of embryos for each assay were also shown. **(C)** Marker gene expression profiling by *in situ* hybridization in embryos at the indicated stages. Scale bar, 250 μm . **(D)** Marker genes expression profile in each dissected part of the embryo by qPCR analysis. **(E, F)** Reproducibility of ChIP-seq of H3K27me3 **(E)** and reduced representation bisulfite sequencing **(F)** data.

Supplementary information, Figure S2

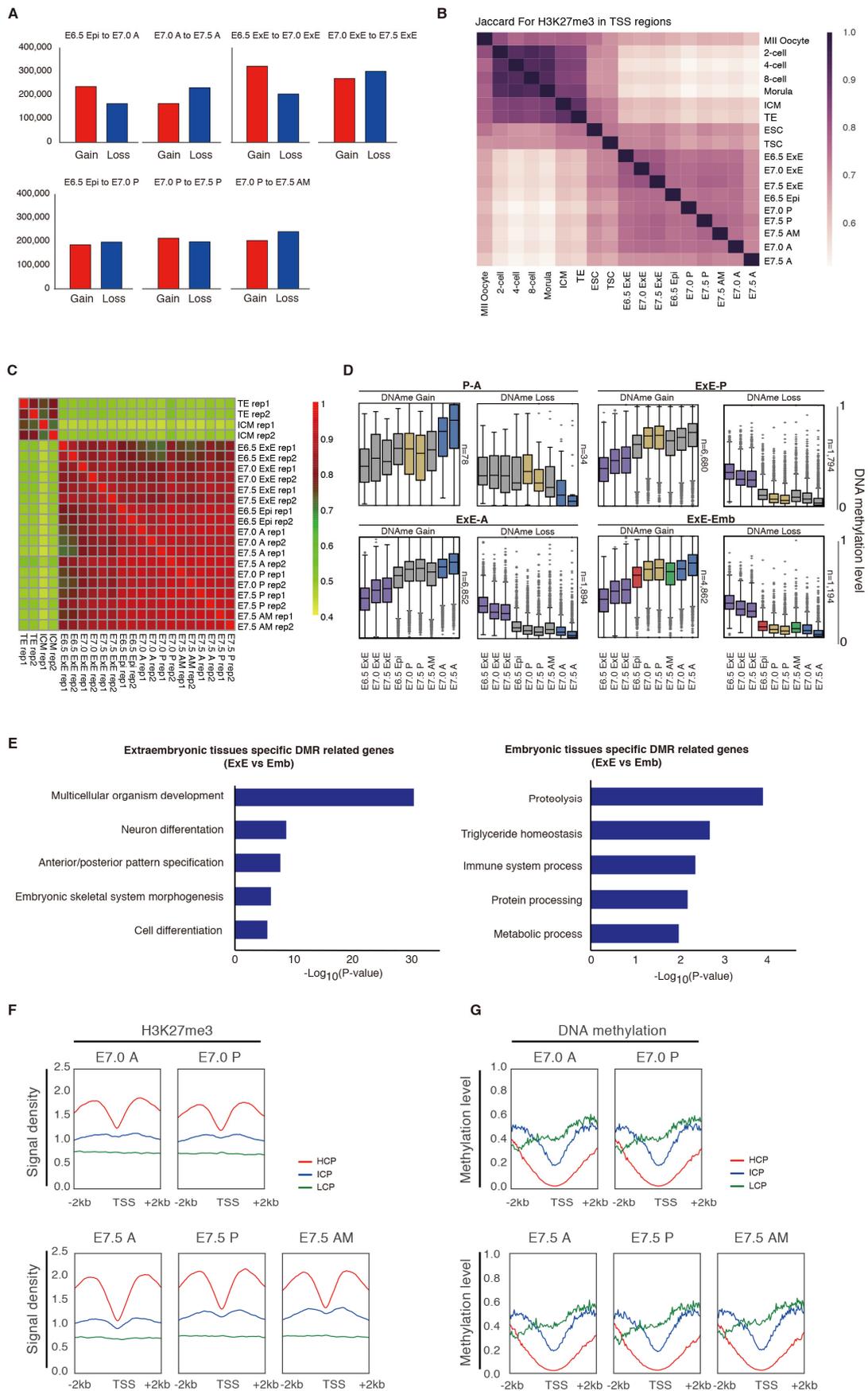


Figure S2 Global dynamics of H3K27me3 and DNA methylation during mouse embryo development. **(A)** Bar plot showing the number of 200 bp bins with gain or loss of H3K27me3 during the development of the gastrula. **(B, C)** Pearson correlation coefficients of H3K27me3 modification pattern **(B)** and DNA methylation **(C)** of samples from pre-implantation to post-implantation embryos. The published data of H3K27me3 enrichment [1] and DNA methylation [2] in pre-implantation embryos were used in these analyses. **(D)** The distribution of DNA methylation level in differentially methylated regions (DMRs, change in methylation > 0.15 , q-value < 0.05) between different regions of the post-implantation embryo. **(E)** Gene ontology (GO) analysis of the genes which show differential methylation level between the embryonic and extraembryonic regions of the embryo. **(F)** Sequence preference of H3K27me3 and DNA methylation for different CpG content promoters in intra-embryonic cells.

Supplementary information, Figure S3

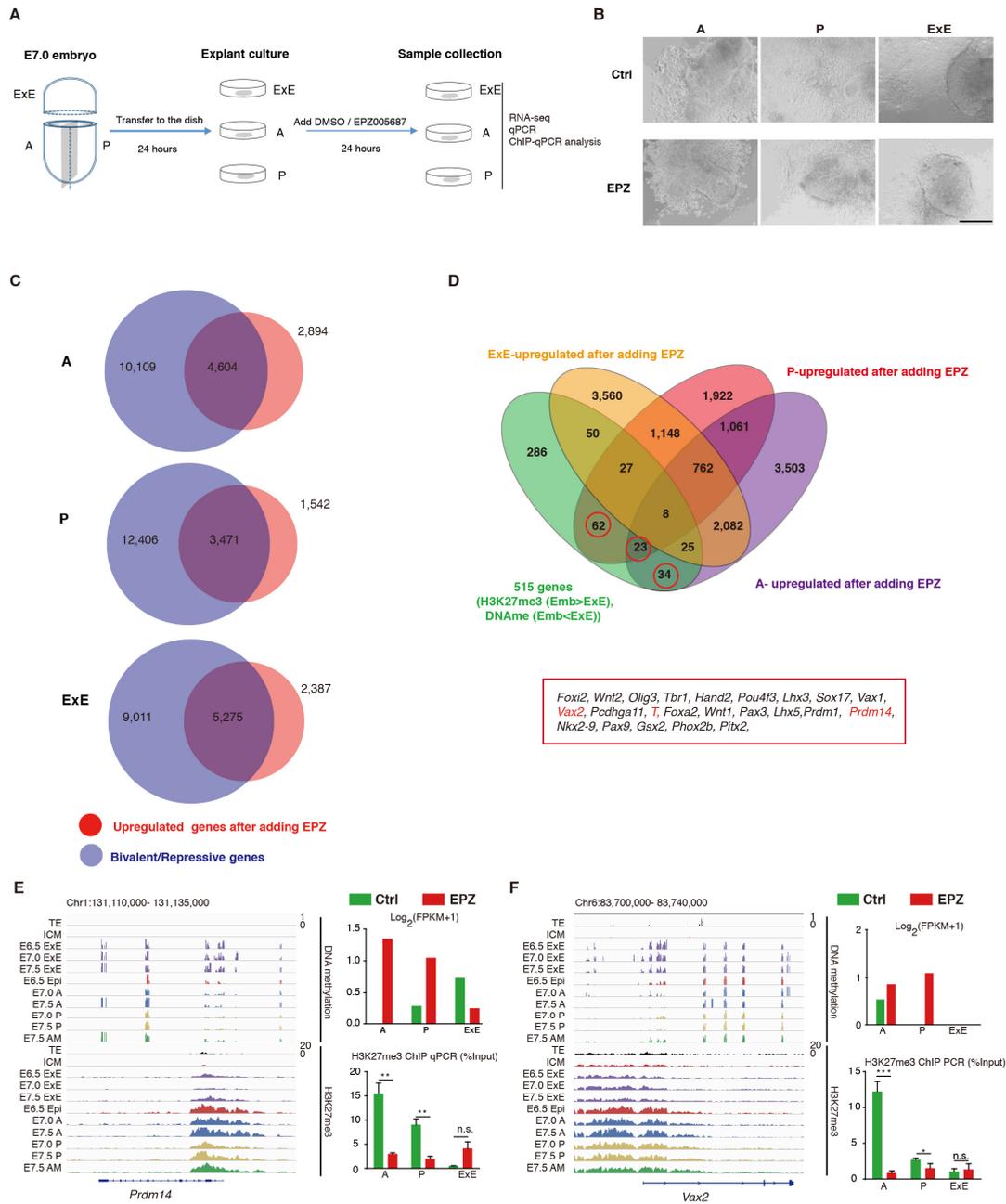


Figure S3 Epigenetic modulation of H3K27me3 triggers different responsiveness in extraembryonic and embryonic cells. **(A)** The scheme showing the procedure of H3K27me3 modulation in a mouse embryo explant culture system. **(B)** Representative images showing the morphology of anterior (A), posterior (P) and extraembryonic (ExE)

explants without (Ctrl, up) or with (EPZ, down) the addition of EPZ005687. Scale bar, 250 μm . **(C)** Venn diagrams showing the overlap between bivalent/repressive genes and upregulated genes after EPZ treatment in each sample. Upregulated genes are defined as genes with expression fold change (FPKM) > 2 . **(D)** Venn diagrams showing the expression changes after the treatment of EPZ. Numbers of each group of genes were notified. Representative genes are notified with red circle and listed. **(E, F)** The genome browser snapshot of DNA methylation and H3K27me3, gene expression changes, H3K27me3 enrichment changes of *Prdm14* **(E)** and *Vax2* **(F)**. $n = 3$; Student's *t*-test, $*P < 0.05$, $**P < 0.01$, $***P < 0.001$.

Supplementary information, Figure S4

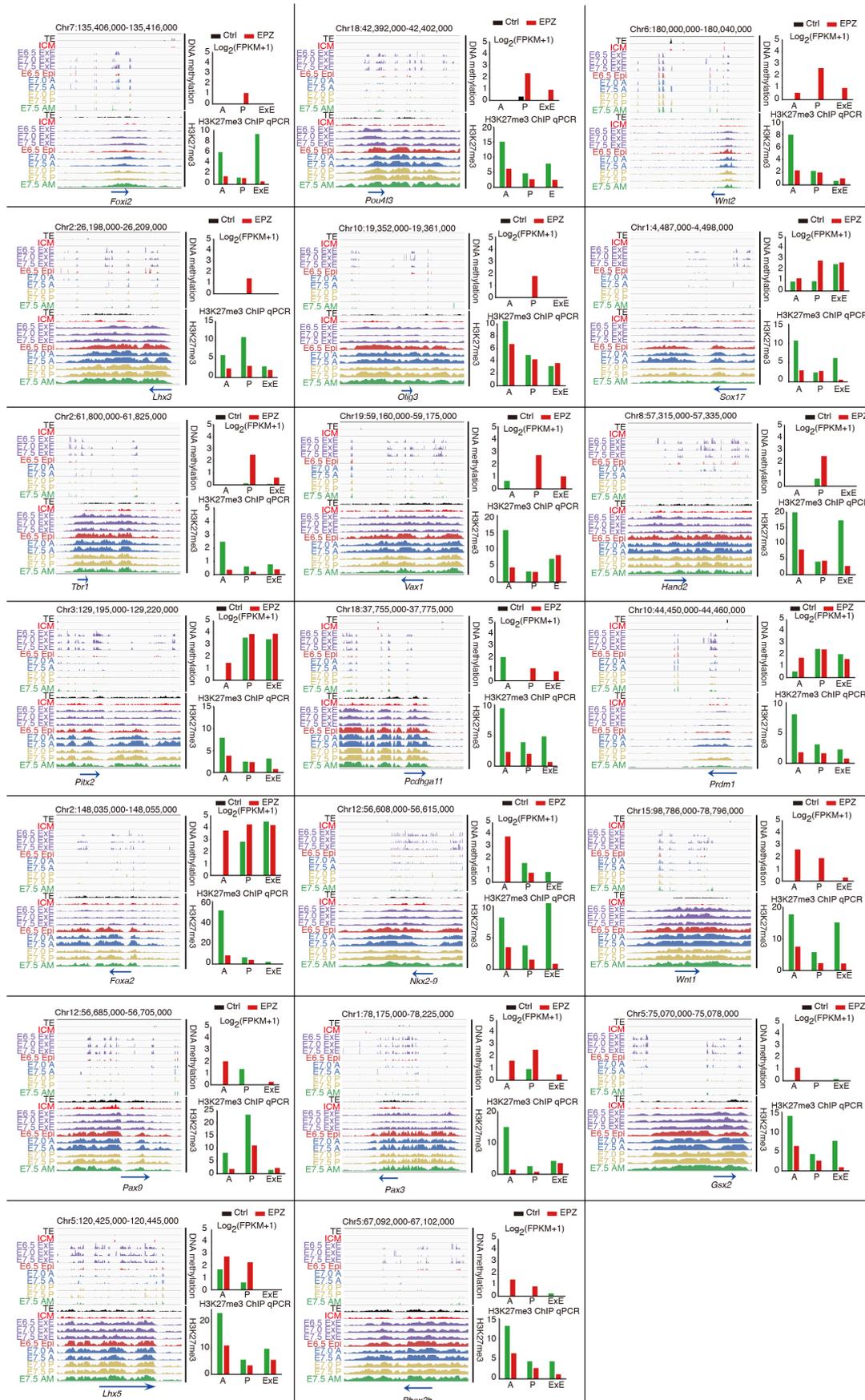


Figure S4 The genome browser snapshot, gene expression change and H3K27me3 change of representative development-related genes.