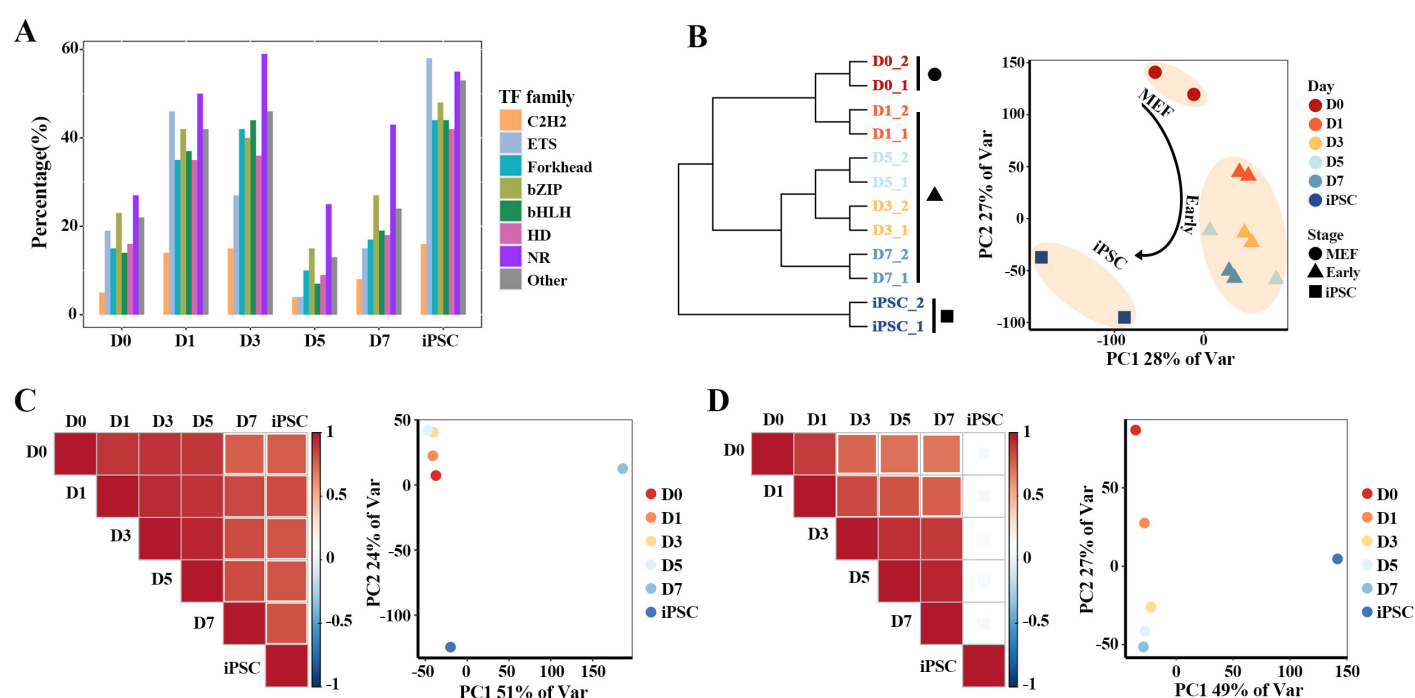


## Supplements

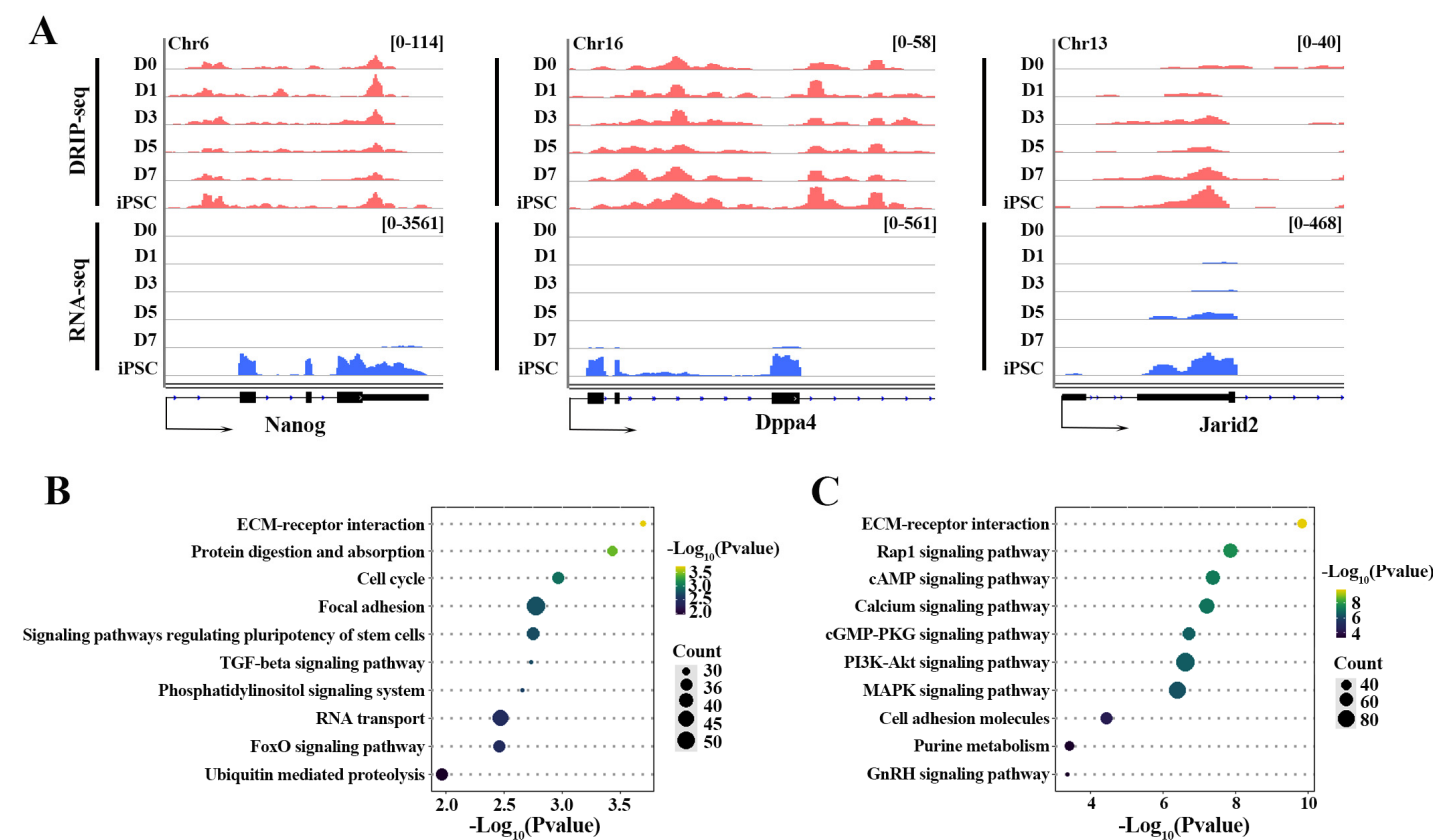
# The Cumulative Formation of R-loop Interacts with Histone Modifications to Shape Cell Reprogramming

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## Supplementary Figures



**Figure S1.** Distribution of R-loops on different elements and analysis of histone modification patterns. **(A)** The distribution of R-loop peaks on different TF family. **(B)** Hierarchical clustering (left) and Principal component analysis (PCA, right) of global transcriptome at different reprogramming stages. Black arrow represents the trajectory of MEF reprogramming to the iPSC state. **(C)** Correlation analysis (left) and PCA (right) of global H3K4me3 binding signals at different reprogramming stages. **(D)** Correlation analysis (left) and PCA (right) of global H3K27me3 binding signals at different reprogramming stages.



**Figure S2.** KEGG pathway enrichment analysis of co-differential genes. **(A)** Representative genome browser snapshot of R-loop signals and genes expression levels during reprogramming progress. **(B)** The top 10 significant KEGG pathways (P value < 0.01) for up-regulated genes with up-regulated R-loop signals (n = 3689, as shown in Figure 2E) between adjacent reprogramming stages. **(C)** The top 10 significant KEGG pathways (P value < 0.01) for down-regulated genes with down-regulated R-loop signals (n = 3290, as shown in Figure 2F) between adjacent reprogramming stages.

