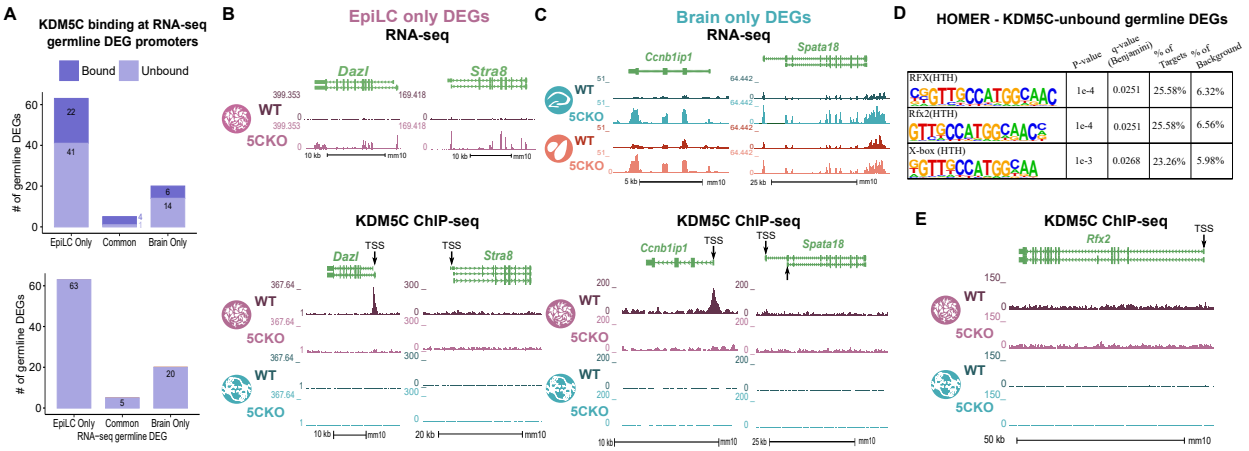
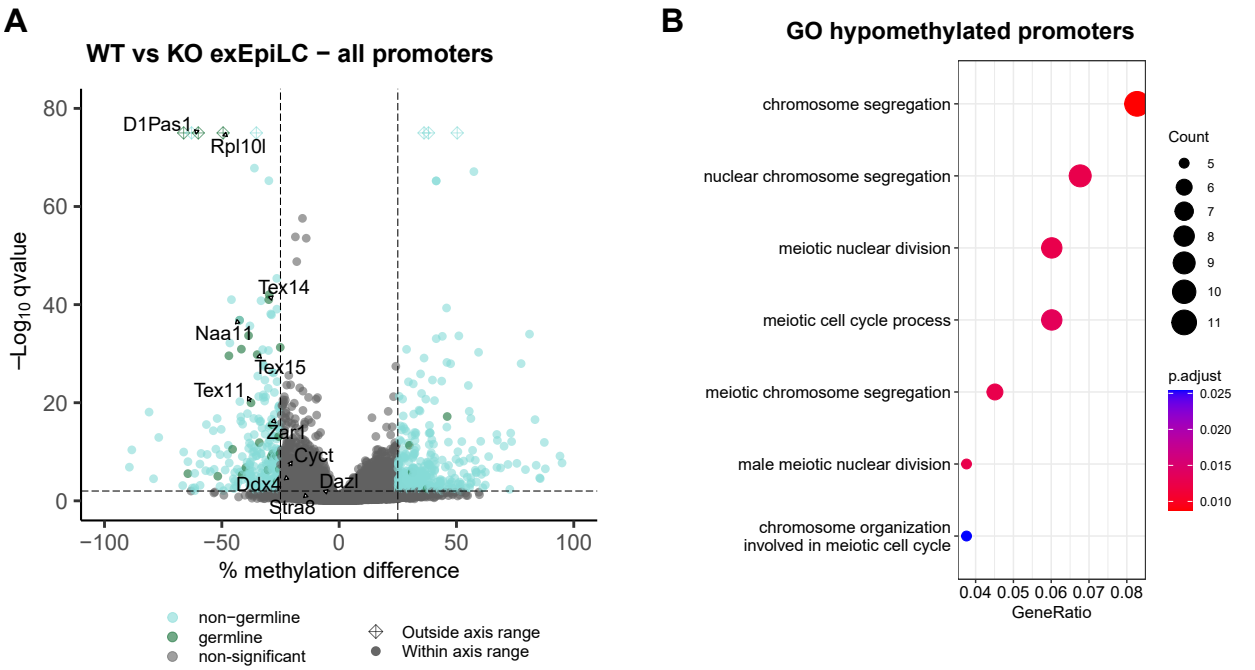
Supplement - Erosion of somatic tissue identity with loss of the X-linked intellectual disability factor KDM5C



Supplementary Figure 1: KDM5C binds to a subset of germline RNA-seq differentially expressed genes. A. Bar graph of the number of germline-enriched DEGs with promoter KDM5C ChIP-seq peaks in wild-type EpiLCs (Top) and PNCs (Bottom). RNA-seq DEGs were classified as shared betwen EpiLCs and the brain (Common), unique to EpiLCs (EpiLC Only), or unique to one or multiple brain regions (Brain Only). **B.** Average bigwigs of two example RNA-seq DEGs dysregulated in EpiLCs but not the brain, *Dazl* and *Stra8*. Top is the RNA-seq tracks for wild-type (WT) and *Kdm5c*-KO (5CKO) EpiLCs, bottom is the KDM5C ChIP-seq tracks, with the annotated transcription start site (TSS) for each gene. **C.** Same as B but for two example DEGs only dysregualted in the brain and not expressed in EpiLCs, *Ccnb1ip1* and *Spata18*. **D.** HOMER motif analysis of all KDM5C-unbound germline DEGs shows signficant enrichment of multiple RFX members and their X-box motif. **E.** KDM5C ChIP-seq shows no KDM5C accumulation at the *Rfx2* promoter in EpiLCs or PNCs.



Supplementary Figure 2: [Loss of KDM5C impairs CpG methylation of germline gene promoters. A. Volcano plot of whole genome bisulfite sequencing (WGBS) for all gene promoters in wild-type (WT) versus *Kdm5c*-KO extended EpiLCs (exEpiLCs). Significantly differentially methylated promoters (q < 0.01, |methylation difference| > 25%). Germline promoters highlighted in green, non-germline promoters in light blue, non-significant promoters in gray. **B.** enrichPlot gene ontology of all promoters significantly hypomethylated in *Kdm5c*-KO exEpiLCs.