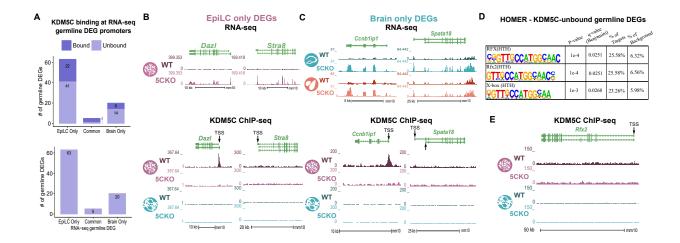
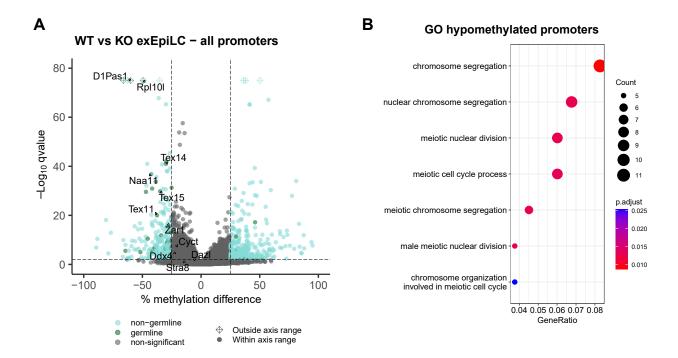
- ¹ Supplement Erosion of somatic tissue identity with loss of the
- 2 X-linked intellectual disability factor KDM5C

3



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 significant 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.