

Description of Additional Supplementary Files

Supplementary Data 1. Reciprocal intersection of ReGenT-seq sub-screens. The ROAST gene set analysis (Wu et al., 2010) ($\text{FDR} < 0.25$) is used to rank the effect of multiple shRNAs targeting the same gene. Score is defined as $-\log(\text{Pvalue})$ of genes $\times$ (number of enriched-number of depleted shRNAs), see methods.

Supplementary Data 2. Overlap of gene hits from Viability screens 1 and 2. The overlap was assessed using Fisher's exact test.

Supplementary Data 3. Overlap of differentially expressed genes in CBX3, KMT5C and EHMT2 knockdown cells versus control cells from RNA-seq ($\text{FDR} < 0.05$). (relative to Fig.2A)

Supplementary Data 4. Overlap between CBX3 ChIP-seq targets and the expression profile of EpSCs. (relative to Fig.4B)

Supplementary Data 5. Overlap between CBX3 RNA-binding targets and CBX3-mediated gene regulations. (relative to Fig.4K)

Supplementary Data 6. Differentially expressed genes in protrusion versus nuclear and cytoplasmic fractions, and in CBX3 knockdown versus scramble control cells. (relative to Fig.5E). Differential subcellular expression analysis was performed using the edgeR GLM testing framework with quasi-likelihood F-test (QLF)

Supplementary Data 7. Oligonucleotides used in this study.

Supplementary Data 8. Antibodies used in this study.