## Supplementary information, Fig. S6



## Supplementary information, Fig. S6 ZNF689 regulates LINE-1 activity by binding to its promoter.

a Box plots showing the expression differences of siNC and siZNF689 for different repetitive elements. LINE, long interspersed element; LTR, long terminal repeats; RC, rolling circle; DNA, DNA repeat elements. b LINE-1 (ORF2) transcript levels determined by RT-qPCR in shNC- and shZNF689expressing cells. c Western blot analysis of LINE-1 ORF1p and ORF2p proteins in shNC and shZNF689 cells. d RT-qPCR analysis of the relative LINE-1 (5'-UTR for Hs578T; ORF2 for AT3) genomic DNA content in shNC and shZNF689 cells. e Dual-luciferase assay showcasing LINE-1 promoter activity in HEK293T cells. f ATAC-seq tracks demonstrating the changes in accessibility of the fulllength LINE-1 promoter after ZNF689 knockdown in LM2 cells. g ChIP-qPCR assessment of ZNF689 enrichment at seven LINE-1 regions in LM2 cells expressing Flag-ZNF689. h Metaplots showing enrichment peaks of Flag-ZNF689 ChIP-seq in the full-length LINE-1 promoter in LM2 cells. i ChIP-seq tracks depicting the binding of ZNF689 at the full-length LINE-1 promoter in LM2 cells. j Comparison of LINE-1 expression differences between the high and low ITH groups in the FUSCC and TCGA cohort. k Co-IP analysis of SETDB1, DNMT3B, HP1 $\alpha$ , HP1 $\gamma$ , and SUV39H1 with endogenous ZNF689 protein in LM2 cells. I Western blot analysis of TRIM28 and SETDB1 protein levels after ZNF689 knockdown. P values were determined using one-way ANOVA (**b**, **d**), two-tailed unpaired Student's t tests (**e**, **g**) and Wilcoxon tests (**h**, **j**). ns, not significant; \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001.