

**Supplementary Figure S6. Genome-wide H3K4me3 and RNAPII changes after treatment with JQKD82 or knockdown of KDM5A in MM.1S cells**

**A,** MA plots representing global increase in H3K4me3 level after treatment with 1 µM of JQKD82 for 48 h in MM.1S cells. Data are separated into transcriptional start site (TSS) distal (left) and TSS proximal (right). H3K4me3 level was measured by spike-in normalized ChIP-Rx. Color scale indicates degree of overlapping points on the scatter plot, with dark blue showing low-numbers of overlapping points, while white-gold color indicates the greatest amount of point overlap (and, high data density).

**B,** Absolute increase in H3K4me3 level is greater at TSS proximal sites (combining both -1 nucleosome and +1 nucleosome regions) compared to TSS distal sites after treatment with 1 µM of JQKD82 for 48 h in MM.1S cells. Left shows absolute changes (delta) and on the right shows the log2 fold changes (L2FC). P values were calculated with a two sided t-test with Welch’s correction.

**C,** ChIP-Rx metagene plot of H3K4me3 signal at TSS for genes downregulated, or not by JQKD82, after knockdown of KDM5A or control shRNA (shLuc) in MM.1S cells.

**D,** ChIP analysis showing CDK7 or CDK9 occupancy at the MYC target gene loci after treatment with 1 µM of JQKD82 or DMSO for 48 h in MM.1S cells. Normal rabbit IgG was used as negative control for ChIP. Percent recovery over the input was determined by quantitative PCR. Data represent mean ± s.d. of triplicate measurements. \**P* < 0.05, \*\**P* < 0.01 compared with DMSO-treated cells; unpaired Student’s t-test.

**E,** Distribution of RNAPII to measure pausing/elongation at all genes after 1 µM of JQKD82 or DMSO for 48 h in MM.1S cells

**F,** Traveling ratio of RNAPII after JQKD82 treatment compared with DMSO treatment (left panel) or after knockdown of KDM5A, compared with control shRNA knockdown (right panel), in MM.1S cells. *P* value was calcuated using a two sample t-test with Welch’s correction. The TSSR, the transcriptional start site region, begins -30 bp upstream of the TSS and ends 300 bp after the TSS.

**G,** Scatter Plot of ChIP-seq analysis on RNAPII Ser5p on the gene body versus pausing index after JQKD82 treatment compared to DMSO.