**[Supplementary Figure 1] Schematic of exon-intron structure of KMT2B in chromosome 19 and KMT2D transcript in chromosome 12 (GRCh37/hg19)**

**Supplementary Figure 1. [a]** Exon (37 exons) and intron position (including cDNA and amino acid position) of KMT2Btranscript (NM\_014727), indicating the position of 10 KMT2B samples (5 frameshift deletion, 3 frameshift duplication, 1 splice variant, and 1 stop-gain mutation). **[b]** Exon (54 exons) and intron position of KMT2Dtranscript (NM\_003482). The location of 10 KMT2D samples (1 splice variant, 3 stop-gain mutation, and 6 frameshift mutation) is specified in the figure. Transcript information is from *Ensembl* (https://grch37.ensembl.org/index.html).

**[Supplementary Figure 2] DMPs showing significant GOM (gain of methylation) or LOM (loss of methylation) in DYT-KMT2B (nDMP=1,812) and KS1 samples (nDMP=89)**

Supplementary Figure 2. Scatter plot of significant **[a]** 1,812 DMPs (FDR < 0.05) in DYT-KMT2B cohort and **[b]** 89 DMPs (FDR < 0.05) in KS1 cohort. Red dots indicate GOM (above control median 3SD confidence interval), blue dots represent LOM (below control median 3SD confidence interval), and grey dots indicate not significant DMPs.

**[Supplementary Figure 3] Genome-wide DNA methylation signature of KS1 samples without KMT2D\_5 sample (nKS1=9, ncontrol=29)**

 **Supplementary Figure 3.** **[a]** Multidimensional scaling (MDS) plot is created based on 136 significant DMPs (FDR < 0.05). **[b]** Unsupervised clustering result of 9 KS1 samples. Hierarchical clustering dendrogram is shown above the annotation bar. Methylation value ranges from 0 to 1 (0 is unmethylated and 1 is methylated DMPs). Heatmap row indicates each CpG (hierarchical clustering by a complete linkage method, NOT sorted by location). 41.9 % of DMPs (57/136) showed GOM patterns while 12.5% (17/136) of DMPs showed LOM patterns.

**[Supplementary Figure 4] Methylation profiling of significant gain– or loss– of methylation in both DYT-KMT2B and KS1 cohort (nDYT-KMT2B=10, nKS1=9, ncontrol=29)**

**Supplementary Figure 4.** From **Figure 2b**, among 677 DMPs, only 505 DMPs within 21 CpG Islands are represented. Gain of methylation (GOM; red) and Loss of methylation (LOM; blue) patterns for 10 DYT-*KMT2B* samples and 9 KS1 samples are shown in this figure. GOM are the sites above median of 29 controls’ 3SD confidence interval and LOM are the area below median of 29 controls’ confidence interval. Interestingly, both of cohorts showed mostly significant GOM patterns. No CpG island region has LOM pattern in a DYT-KMT2B cohort but 2.77% (14/505 DMPs) of KS1 cohort showed significant LOM patterns. Specific DMP names, p-values, and different methylation levels are summarised in **Supplementary Table 2 and 3.**