

## Description of Additional Supplementary Files

**File name:** Supplementary Data 1

**Description:** STARS output files for sgRNAs targeting DNMT3B

**File name:** Supplementary Data 2

**Description:** Custom DNMT1/3B CRISPR pooled sgRNA library

**File name:** Supplementary Data 3

**Description:** Raw counts for NGS results, binning of DNMT1 and DNMT3B CRISPR sgRNAs, and original chip file for custom DNMT1/3B CRISPR pooled sgRNA library.

**File name:** Supplementary Data 4

**Description:** Individual sgRNA sequences used for mutational analysis

**File name:** Supplementary Data 5

**Description:** Raw data files for data shown in Figure 1.