

## Description of Additional Supplementary Files

File Name: Supplementary Data 1

Description: **GW-CRISPR KO screen analysis results**

Analysis of GW-CRISPR screen using CasTLE. See excel spreadsheet.

File Name: Supplementary Data 2

Description: **GE-CRISPR KO screen analysis results**

Analysis of GE-CRISPR screen using CasTLE. See excel spreadsheet.

File Name: Supplementary Data 3

Description: **Single-cell RNA-seq from single-cell RNA-seq comparing WT vs *Tada2b* KO cells**

DEG analysis of single-cell RNA-seq data comparing *Tada2b* KO and WT cells separated by cell type. See excel spreadsheet.

File Name: Supplementary Data 4

Description: **Single-cell RNA-seq analysis results comparing WT vs *Taf5l* KO cells**

DEG analysis of single-cell RNA-seq data comparing *Taf5l* KO and WT cells separated by cell type. See excel spreadsheet.

File Name: Supplementary Data 5

Description: **Bulk RNA-seq analysis results comparing *in vivo* control vs *Taf5l* KO and *Tada2b* KO cells**

DEG analysis of bulk RNA-seq data comparing *Tada2b*-KO and *Taf5l*-KO *in vivo* HSPCs compared WT HSCs. See excel spreadsheet.

File Name: Supplementary Data 6

Description: **Bulk RNA-seq analysis results for *in vitro* experiments**

DEG analysis of bulk RNA-seq data comparing *Tada2b*-OE, *Tada2b*-KO, *Ifnar*-KO, *Ifnar*-*Tada2b*-DBKO and control HSPCs. See excel spreadsheet.

File Name: Supplementary Data 7

Description: **ATAC-Seq and Chipmentation data of *Tada2b* KO and Control HSPCs**

Differential Peak analysis, HOMER enrichment motif analysis and Gene enrichment terms for ATAC-seq data, and H2Bub and H3K9ac Chipmentation data comparing *Tada2b* KO and control HSPCs .

File Name: Supplementary Data 8

Description: **Bulk RNA-seq analysis results for HSPCs treated with KAT2A/B inhibitor (GSK699).**

DEG analysis of bulk RNA-seq data of HSPCs treated with KAT2A/B inhibitor (GSK699) and KO of *Tada2b* along untreated WT HSPCs and *Rosa26* KO controls.

File Name: Supplementary Data 9

Description: **Bulk RNA-seq analysis results for *in vivo* experiments comparing *TADA2B*-KO, *TAF5L*-KO, *TADA1*-KO MDS-L cells compared to control MDS-L cells**

DEG analysis of bulk RNA-seq data comparing *TADA2B*-KO, *TAF5L*-KO, *TADA1*-KO MDS-L cells compared to control MDS-L cells.