



Supplementary Figure 1. (a) Schematic representation of human KAT6A and KAT6B proteins with amino acid lengths. (b) Schematic representation of the yeast two-hybrid system performed to identify PRMT2 as a partner of KAT6A. (c) Western Blot analysis after co-transfection followed by co-immunoprecipitation of either Myctagged KAT6A or citrine-tagged PRMT2 protein in HEK293 cells. The input fraction represents 5% of the total protein extract. The presented blot is representative of three independent experiments.

а



**Supplementary Figure 2**. (a) Mutation profile of the 105 AML patient exomes from *the Leucegene Project* depending on their *PRMT2* expression for a subset of frequently mutated genes in AML. Blue: mutated gene; grey: non mutated gene. (b) Box plots showing NF- $\kappa$ B-related gene expression of *PRMT2*<sup>low</sup> and *PRMT2*<sup>high</sup> patients in the *BeatAML* (n = 30 in each group) cohort. Error bars represent mean  $\pm$  SD. Multiple unpaired t tests with p values indicated in the graphs; \*p < 0.05; \*\*p < 0.01; \*\*\*\*p < 0.0001 (c) GSEA plot for the "TNFA signaling via NFKB" hallmark on the *BeatAML* cohort with FDR and nominal p indicated. (d-e) Pearson's correlations of *PRMT2* expression with *FTH1* (d) and *FTL* expression (e) within *the Leucegene Project* cohort (n = 371).



**Supplementary Figure 3.** Flow cytometry analysis showing fluorescence intensity for the CD34, CD33, CD13, CD15, CD14, CD16, CD117, and CD11b surface markers on WT HL-60 and 3 different clones of *PRMT2<sup>KO</sup>* cells. Cells are considered as positive if the mean fluorescence intensity is above 10<sup>2</sup>. The presented graphs are representative of three independent experiments.



**Supplementary Figure 4**. (a) Blood cell counts in  $Prmt2^{-/-}$  or control ( $Prmt2^{+/+}$ ) mice. RBC: red blood cells; WBC: white blood cells; LYM: lymphocytes; GRA: granulocytes; EOS: eosinophiles; MON: monocytes. (b) Flow cytometry analysis on BM showing percentages of B cells (B220<sup>+</sup>), monocytes/neutrophils (Gr-1<sup>+</sup>CD11b<sup>+</sup>), and erythroid cells (Ter-119<sup>hi</sup>) (left) and lineage negative, LK and LSK (right). (c) Flow cytometry analysis of hematopoietic reconstitution of  $Prmt2^{-/-}$  or control BM cells (CD45.2<sup>+</sup>) transplanted into recipient mice (CD45.1<sup>+</sup>) in competition with recipient's cells (1:1 ratio). Number of mice in each group are shown on graphs. All presented data (a-c) are expressed as mean  $\pm$  SD. (d) Morphological analysis of monocytes during differentiation into macrophages. Images from phase-contrast microscopy using an Incucyte<sup>®</sup> S3 Live-Cell Analysis System at magnification x20. (e) Flow cytometry analysis for CD14, CD16, CD64, CD80, CD206, and F4/80 surface markers from unstimulated or 24h LPS-stimulated  $Prmt2^{+/+}$  (grey) or  $Prmt2^{-/-}$  BMDMs (red). Unstained cells are shown in black as negative control. Presented graphs are representative figures from three independent experiments.



CD126 (IL6R)

**Supplementary Figure 5**. (a) Flow cytometry analysis for the IL6 receptor (CD126) from unstimulated or LPSstimulated WT (grey) or *PRMT2<sup>KO</sup>* HL-60 cells (red). Unstained cells are shown in black as negative control. (b) Western Blot analysis of STAT3 after immunoprecipitation of citrine-PRMT2 unstimulated or 24h LPS-stimulated HL-60 cells. The input fraction represents 5% of the total protein extract. The presented blot is representative of three independent experiments.



**Supplementary Figure 6**. (a) Gating strategy for all the presented flow cytometry data, from all events. (b-c) Gating strategies for Supplementary Figure 4b, from the 'single cells 2' gate.



Anti-GFP

Cri Input IP. citine IP. NAC

Anti-MYC





# Full unedited blot for Figure 3a



Anti-PRMT1



Anti-PRMT3

# Full unedited blot for Figure 3a



Anti-CARM1



Anti-PRMT2





Anti-GAPDH

Anti-PRMT5



Anti-pSTAT3



Anti-GAPDH



Anti-STAT3





Anti-GAPDH



Anti-STAT3

## Full unedited blot for Figure 6a





Anti-GAPDH



Anti-STAT3

## Full unedited blot for Figure 6c



Anti-p-SAPK/JNK



Anti-p-ERK1/2



Anti-p-P38

Anti-GAPDH

## Full unedited blot for Figure 6c



Anti-ERK1/2



Anti-SAPK/JNK



Anti-P38

#### Full unedited blot for Figure 6d

			LPS (h) 24	48	
			WT KO	WT KO	
				CNCN	
LPS (h) Ctrl	4	8	70		
PST WT KO	<u>WT КО</u>	WT КО			- 1 A -
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-					
	= =				
LPS (h) 24	48		103 1		1
WT KO	WT KO				
СИСИ	CNCN		LPS (h) <u>Ctrl</u>	4	<u> </u>
			WT KO	<u>WT КО</u>	WT КО
2			СNСN	CNCN	CNCN
			70		

Anti-pSTAT3





Anti-NFKB P65

LPS (h) Ctrl 4 8 wт ко WТ ко WТ ко N C N С Ν с Ν С С Ν С Ν 55 Backy 2 LPS (h) 24 48 WT KO WΤ KO С Ν С Ν С Ν С Ν 55 1) achh3

Anti-ACTB



Anti-GFP



Anti-STAT3