Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Virtual screening and biological evaluation of novel small molecular inhibitors against Protein Arginine Methyltransferase 1 (PRMT1)

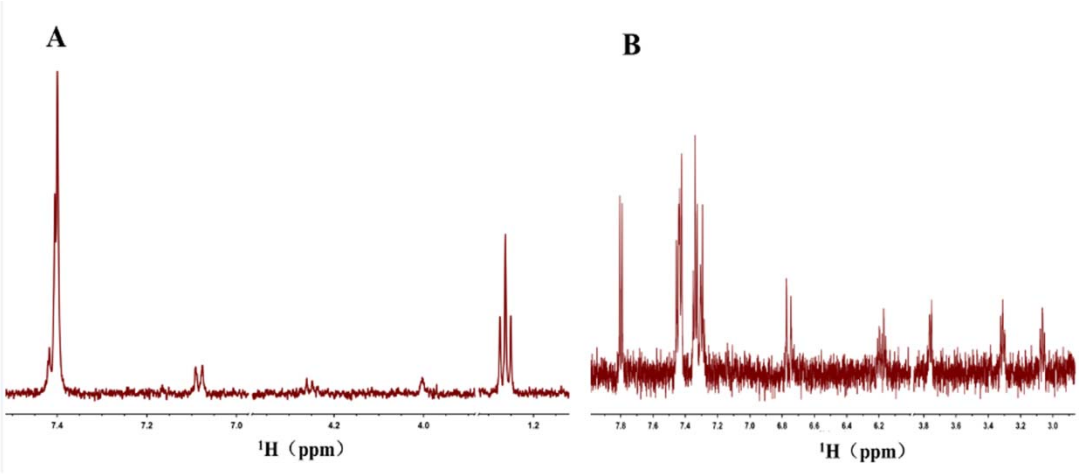

Fig. S1 (A) Saturation transfer difference (STD)-NMR spectra of compound DCLX069 mixed with PRMT1. (B) STD-NMR spectra of compound DCLX078 mixed with PRMT1. The STD-NMR spectra confirmed that both compounds (DCLX069 and DCLX078) could interact with protein PRMT1.

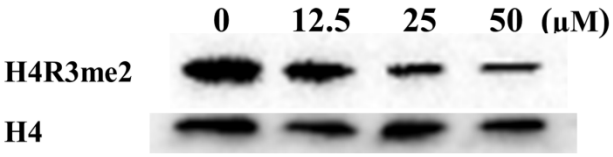

Fig. S2 Western blot for arginine hypomethylation of compound DCLX078.

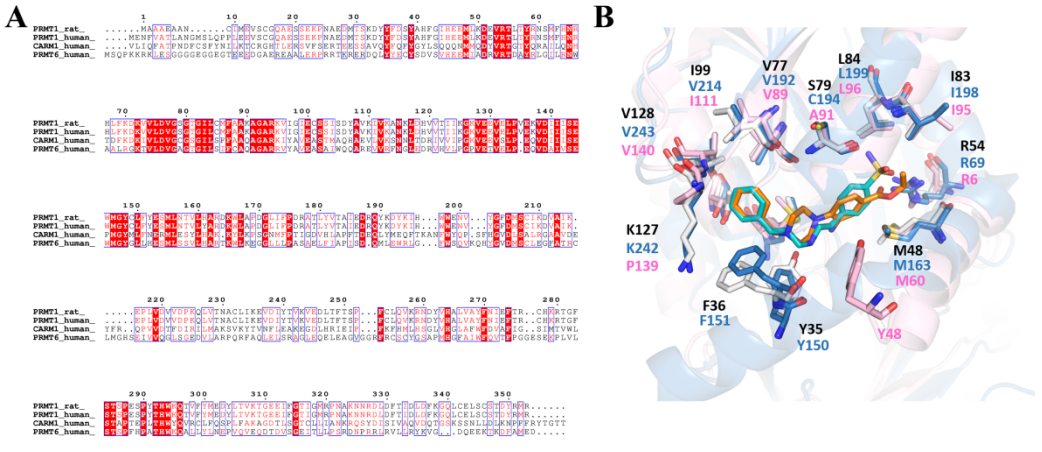

Fig. S3 (A) Sequence alignment of PRMT1 (rat and human), PRMT4 (human) and

PRMT6 (human). (B) Structural superimposition of active sites of PRMT1, PRMT4 and PRMT6. PRMT1 (PDB ID code: IOR8), PRMT4 (3B3F) and PRMT6 (4HC4) are colored grey, mazarine and pink, respectively. DCLX069 and DCLX078 shown in sticks are colored orange and cyan.

Experimental

Histone Hypomethylation

HepG2 cells were treated with DCLX078, the cells are incubated at 37 °C. Appropriate DMSO controls are included. After 72 hours, the supernatant is removed. The cells are resuspended in 500 µl ice-cold PBS and collected in 1.5 ml reaction tubes. The cells were lysed, and boiled at 99 °C for 5 min in sample buffer (50 mM TrisHCl PH 8.0; 150 mM NaCl; 1% NP-40; 0.5% sodium deoxycholate; 0.1% SDS). Lysate were separated with SDS-PAGE, and transferred to PVDF membrane (GE healthcare). The membranes were first incubated with blocking buffer (TBS with 0.05% Tween 20, 5% non-fat milk) for 2 h at room temperature and then incubated overnight at 4 °C in buffer containing primary antibodies respectively. (anti-dimethyl-Histone H4 (Arg3) Asymmetric, Millipore & anti-Histone H4, PTM Biolabs, Inc.). The membranes were washed thrice and incubated with goat anti-rabbit IgG HRP for 2 h. After washing, immunostaining was visualized using FluorChemFC3(Proteinsimple^{TM}).