Supplemental Figure and Figure legend



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Supplemental Figure 1 PRMT6 binds to MSH2 in response to DNA damage

(A) Immunoblot analysis of MSH2 and PRMT6 after immunoprecipitation using anti-Flag antibody derived in 293T cells treated with DMSO, CDDP (5 μ M), 6-TG (5 μ M) and MNNG (5 μ M). CDDP, cis-Diamminedichloroplatinum), 6-TG, 6-Thioguanine and MNNG, N-methyl-N'-nitro-N-nitrosoguanidine. (B) Representative images and quantification of cell apoptosis analyzed by FACS. Unpaired t test was used to determine statistical significance. *, **, *** means p < 0.05, p < 0.01, and p < 0.001.



Supplemental Figure 2 PRMT6 loss in mice does not affect body weight, colon length and mucosa integrity

(A) Quantification of body weight in WT and $Prmt6^{-/-}$ mice (n=6). (B) Gross image and quantification of colon length in indicated mice (n=6). Scale bar, 1 cm. (C) HE staining of colon from indicated mice. Scale bar, 50 µm. Unpaired t test was used to determine statistical significance. *, **, *** means p < 0.05, p < 0.01, and p < 0.001.



Supplemental Figure 3 MMR genes were downregulated in CRC cells treated with EPZ020411

Determination of MMR gene expression in cells treated with EPZ020411 for 12h. *P* values were determined by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparisons test. *, **, *** means p < 0.05, p < 0.01, and p < 0.001.



Supplemental Figure 4 Sequential gating strategy to identify and quantify immune cell subsets in tumors

After exclusion of doublets, live CD45⁺ cells were gated and the proportion of indicated subpopulations were evaluated.



Supplemental Figure 5 MC38 and CT26T cells treated with PRMT6i or anti-PD1 antibody alone or in combination.

(A) Quantification of cell subsets by FACS in xenografts of CT26T cells (n=5). (B) Gross image and quantification of xenografts of control and PRMT6-depleted CT26 cells in mice with indicated treatment (n=5). Scale bar, 1 cm. (C) Histological analysis of tumor sections from indicated xenografts. Upper, HE staining of indicated tumor sections. Middle & Lower, IHC staining of Ki-67 and CD8 in indicated tumor sections. Scale bar, 50 μ m. (D) Gross image and quantification of xenografts of MC38T cells in mice with indicated treatment. Scale bar, 1 cm. (E) Colon length of mice with AOM/DSS-induced tumor model followed by indicated treatment. *P* values were determined by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparisons test. *, **, *** means p < 0.05, p < 0.01, and p < 0.001.