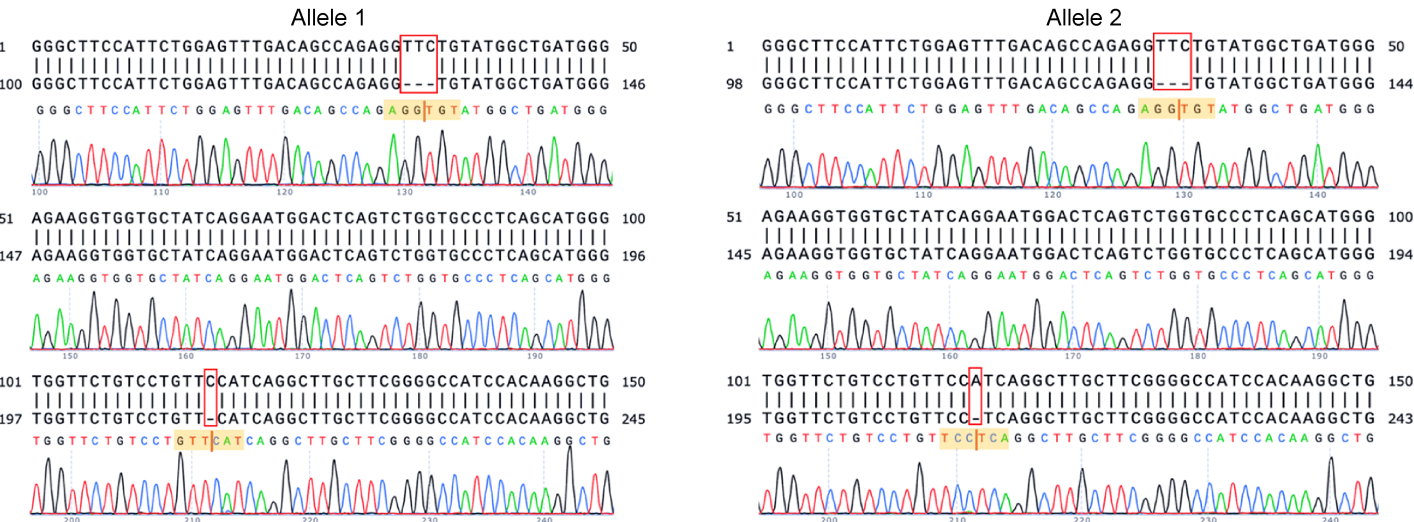


Figure S1

A

CT-26 KO Clone 2



CT-26 KO Clone 2



B

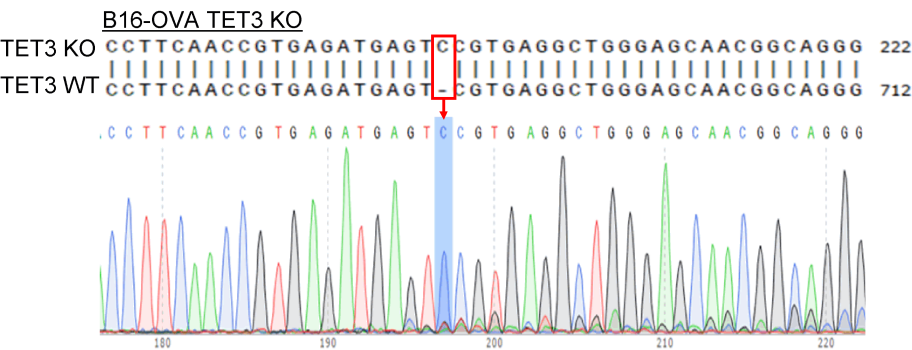
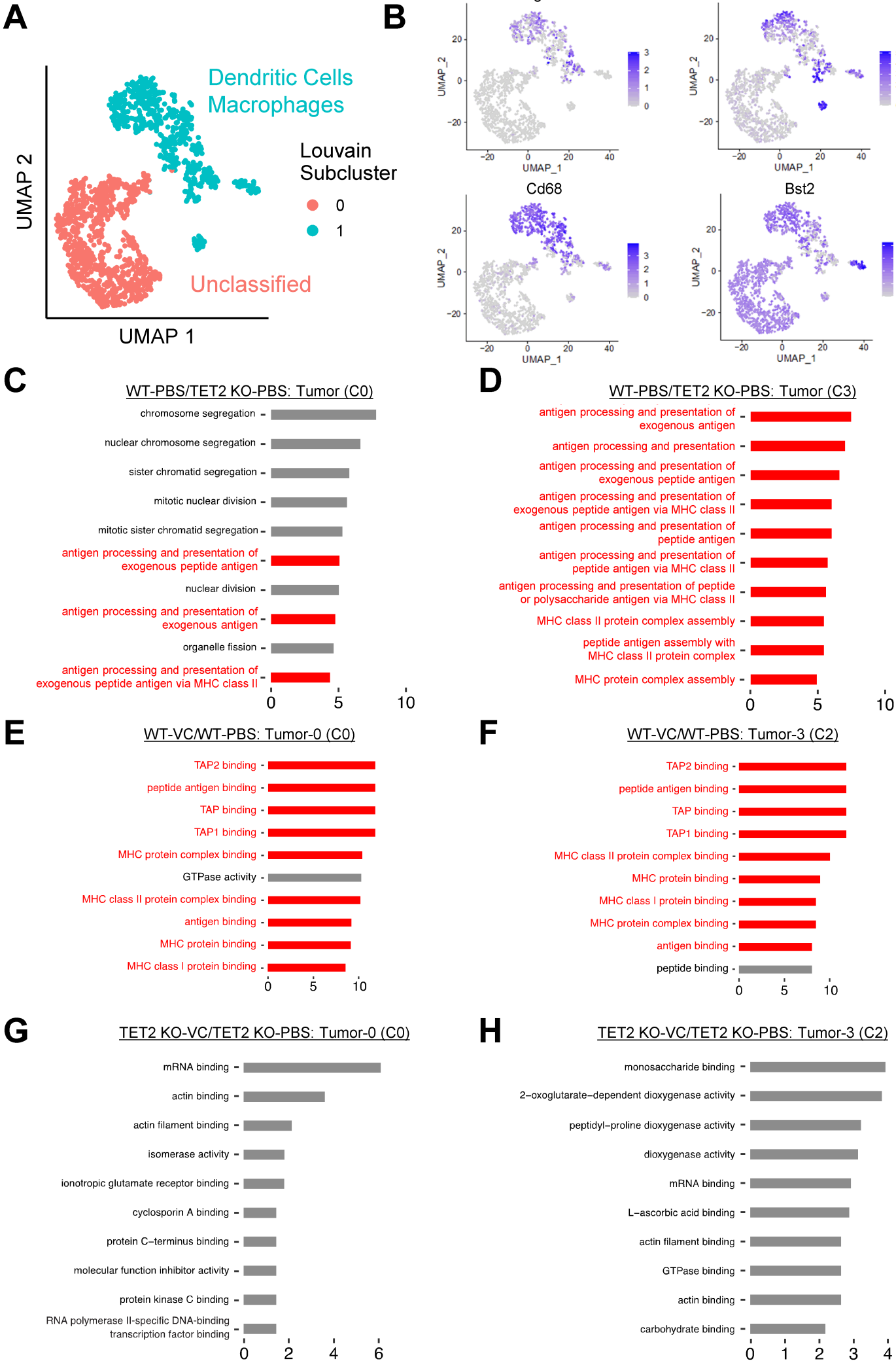


Figure S2



A Volcano plot - WT_VC_WT_PBS cluster^1-grp01

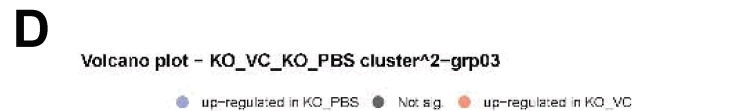


Figure S4

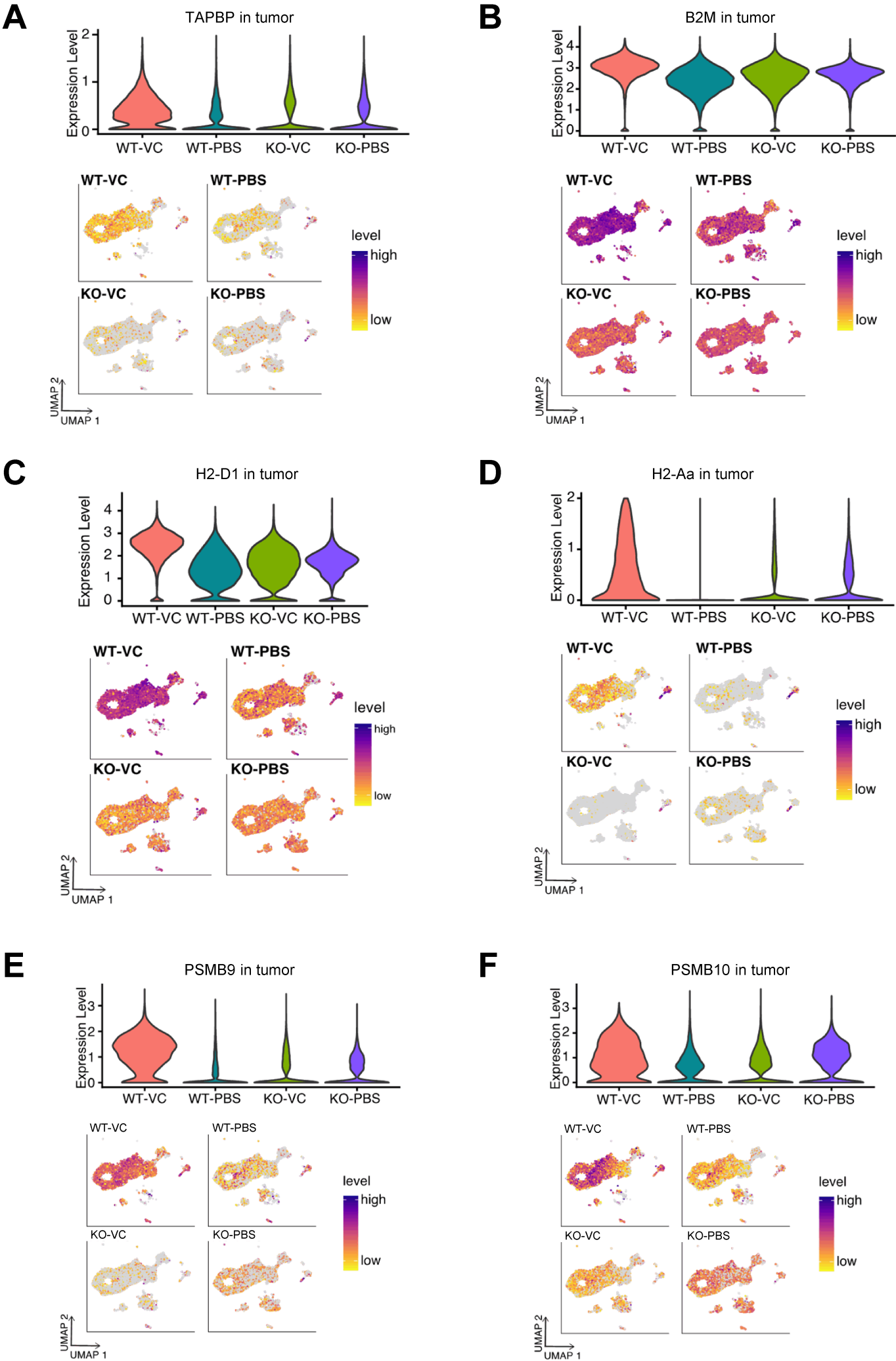
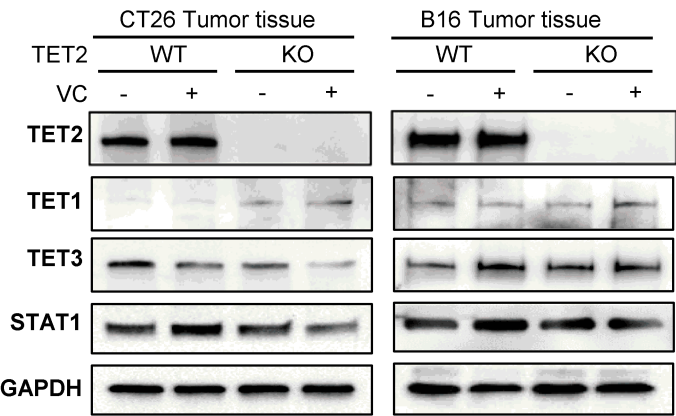
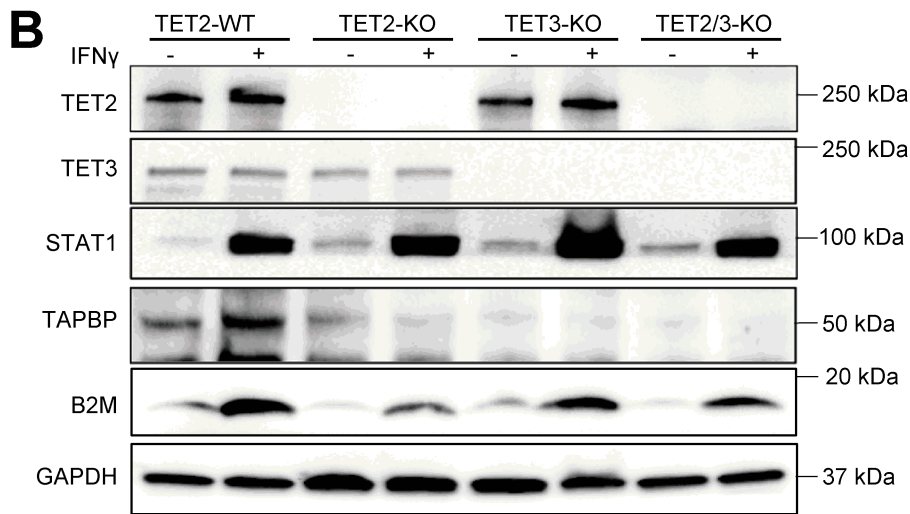


Figure S5

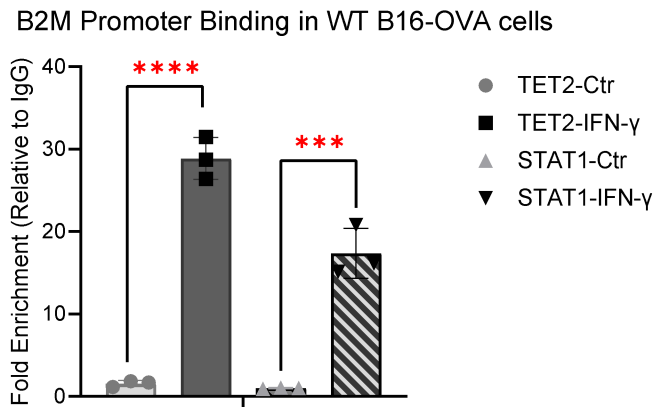
A



B



C



D

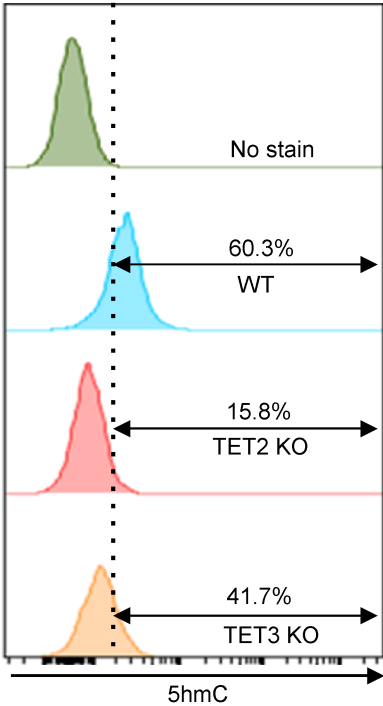


Figure S1. The sequencing confirmation of TET2-KO CT-26 clones.

(A) WT or two TET2-KO CT-26 clones were generated using CRISPR-Cas9 gene editing technique and confirmed by DNA sequencing, the loss-of-function mutations in TET2-KO clones were aligned to WT sequences. (B) TET3 knockout and TET2/TET3 double knockout B16-OVA cells were generated by CRISPR-Cas9 gene editing technique and confirmed by DNA sequencing, the loss-of-function mutations in TET2-KO clones were aligned to WT sequences.

Figure S2. Characterization of Cluster 9. VC induced antigen presentation processes and molecular functions rely on the expression of TET2.

UMAP clustering for group 9 cells (see Fig. 2) (A) based on expression of established markers for dendritic cells and macrophages (B) (63). The top 10 most significantly enriched cellular processes in the WT tumor basal expression compared to TET2-KO in cluster C0 (C) or in cluster C3 (D) were presented based on GO analysis of the top 100 DEGs, and the antigen presentation processes were marked in red. The top 10 most significantly enriched molecular functions after VC stimulation in the WT B16-OVA tumor clusters C0 (E) or C2 (F) and in the TET2-KO tumor cluster C0 (G) or C2 (H) were determined by GO analysis of the top 100 DEGs for each cluster with antigen presenting functions marked in red.

Figure S3. VC induced MHC class I antigen presentation-related gene expression in the WT but not TET2-KO tumor cells.

The top 30 DEGs after VC treatment in WT tumor cluster C1 (A) or WT tumor cluster C2 (B) and TET2-KO tumor cluster C1 (C) or TET2-KO tumor cluster C2 (D) were annotated in the volcano plots according to their adjusted P values and genes involved in the MHC I antigen presentation were marked in red. (E) Representation of DEGs between WT tumor cluster 3 and TET2-KO cluster 3 annotated as volcano plots.

Figure S4. VC induced MHC class I antigen presentation related gene expression in the WT but not TET2-KO tumor cells.

The single-cell expression of MHC class I antigen presenting genes TAPBP (A), B2M (B), H2-D1 (C), H2-Aa (D) and immunoproteasome genes PSMB9 (E), PSMB10 (F) in the WT or TET2-KO B16-OVA tumor tissue treated with PBS control or VC were summarized. The relative expression of genes shown above was calculated by log2-normalized gene counts data. On the UMAP projection, purple indicates high level and yellow indicates low level with quantification presented in the violin plot above.

Figure S5. VC induced MHC class I antigen presentation related gene expression in the WT but not TET2-KO tumor cells.

(A) The expression of the three TET family proteins: TET1, TET2 and TET3 as well as STAT1 in WT or TET2-KO CT26 and B16-OVA tumor tissue as shown by western-blot. (B) Expression of TAPBP and B2M in TET2 WT and KO, TET3 KO, and TET2/3 KO B16-OVA cells following IFN- γ stimulation. (C) ChIP assay at the B2M promoter for TET2 and STAT1, following IFN- γ stimulation of B16 OVA cells. (D) 5hmC levels in WT or TET2-KO or TET3-KO B16-OVA cells as determined by FACS.

Figure 1A, Table

PBS	-				
Anti-PDL1	n.s.	-			
Anti-PDL1 + i.p. 1g/kg VitC	*	n.s.	-		
Anti-PDL1 + i.p. 4g/kg VitC	**	n.s.	n.s.	-	
Anti-PDL1 + i.v. 0.25g/kg VitC	***	n.s.	n.s.	n.s.	-
Anti-PDL1 + i.v. 1g/kg VitC	****	**	**	**	*
	PBS	Anti-PDL1	Anti-PDL1 + i.p. 1g/kg VitC	Anti-PDL1 + i.p. 4g/kg VitC	Anti-PDL1 + i.v. 0.25g/kg VitC

Figure 1B, Table

PBS	-				
Anti-PDL1	**	-			
Anti-PDL1 + i.p. 1g/kg VitC	**	n.s.	-		
Anti-PDL1 + i.p. 4g/kg VitC	****	n.s.	n.s.	-	
Anti-PDL1 + i.v. 0.25g/kg VitC	****	**	n.s.	n.s.	-
Anti-PDL1 + i.v. 1g/kg VitC	****	***	**	*	n.s.
	PBS	Anti-PDL1	Anti-PDL1 + i.p. 1g/kg VitC	Anti-PDL1 + i.p. 4g/kg VitC	Anti-PDL1 + i.v. 0.25g/kg VitC

WT+PBS	-							
WT+VC	n.s.	-						
WT+anti-PDL1	****	****	-					
WT+anti-PDL1+VC	****	****	****	-				
Tet2-KO+PBS	n.s.	-	-	-	-			
Tet2-KO+VC	-	n.s.	-	-	n.s.	-		
Tet2-KO+anti-PDL1	-	-	****	-	n.s.	n.s.	-	
Tet2-KO+anti-PDL1+VC	-	-	****	****	n.s.	n.s.	n.s.	-
	WT+PBS	WT+VC	WT+anti-PDL1	WT+anti-PDL1+VC	Tet2-KO+PBS	Tet2-KO+VC	Tet2-KO+anti-PDL1	Tet2-KO+anti-PDL1+VC

Figure 1D, Table

WT+PBS	-							
WT+VC	n.s.	-						
WT+anti-PDL1	****	**	-					
WT+anti-PDL1+VC	****	****	n.s.	-				
Tet2-KO+PBS	n.s.	-	-	-	-			
Tet2-KO+VC	-	n.s.	-	-	n.s.	-		
Tet2-KO+anti-PDL1	-	-	**	-	n.s.	n.s.	-	
Tet2-KO+anti-PDL1+VC	-	-	-	****	n.s.	n.s.	n.s.	-
	WT+PBS	WT+VC	WT+anti-PDL1	WT+anti-PDL1+VC	Tet2-KO+PBS	Tet2-KO+VC	Tet2-KO+anti-PDL1	Tet2-KO+anti-PDL1+VC

Figure 1E, Table