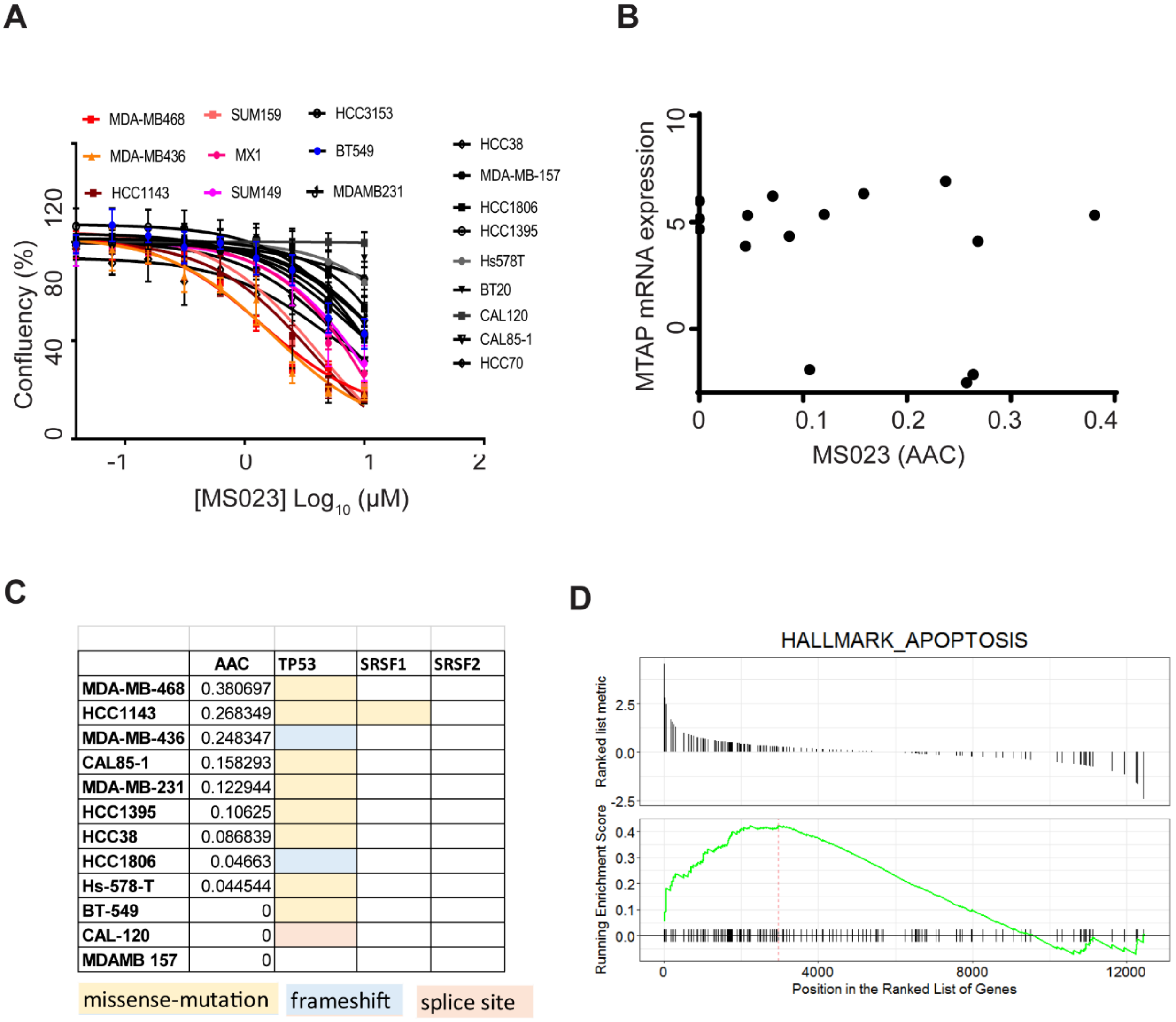
Table S1: *In Vitro* Kd value for indicated chemical probes.

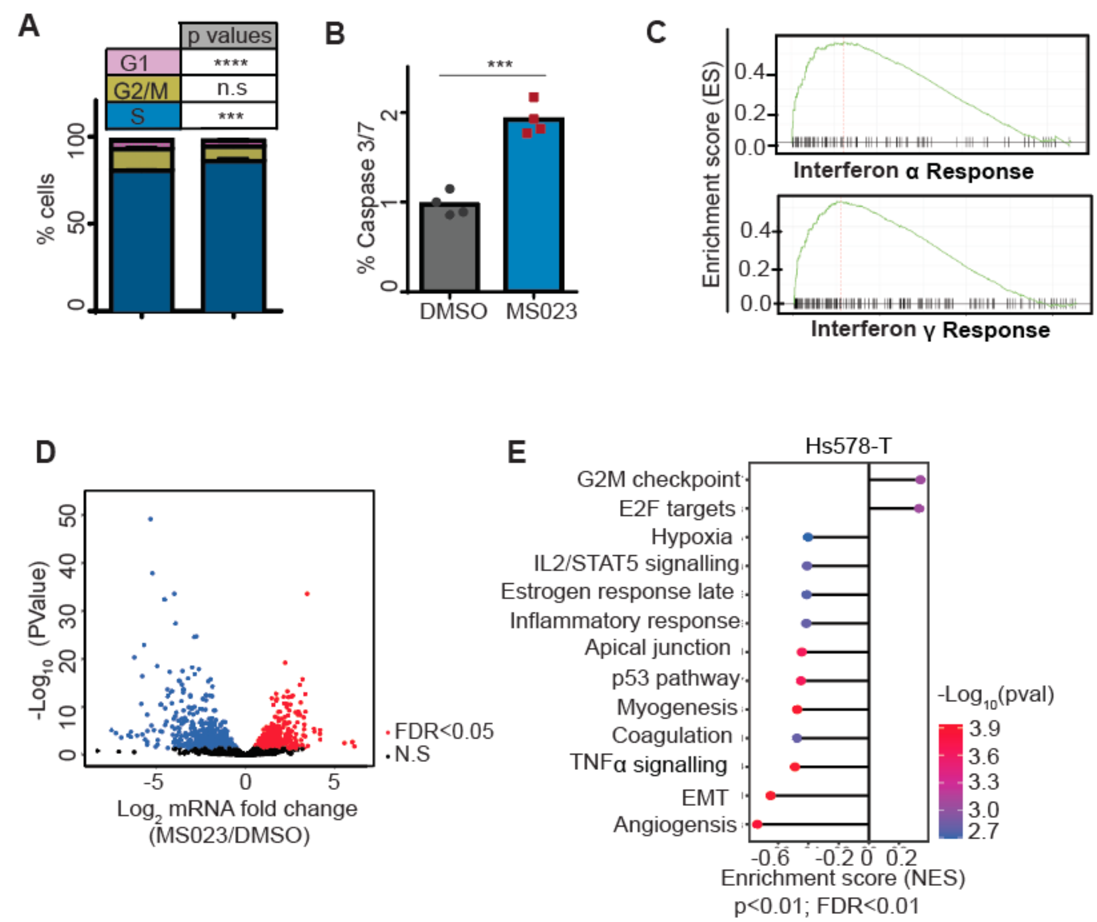
Type I PRMTs	Kd (nM)			
	MS023	SGC707	MS049	TP-064
PRMT1	39			
PRMT3	135	31		
PRMT4	93		44	<10
PRMT6	4		63	
PRMT8	5			



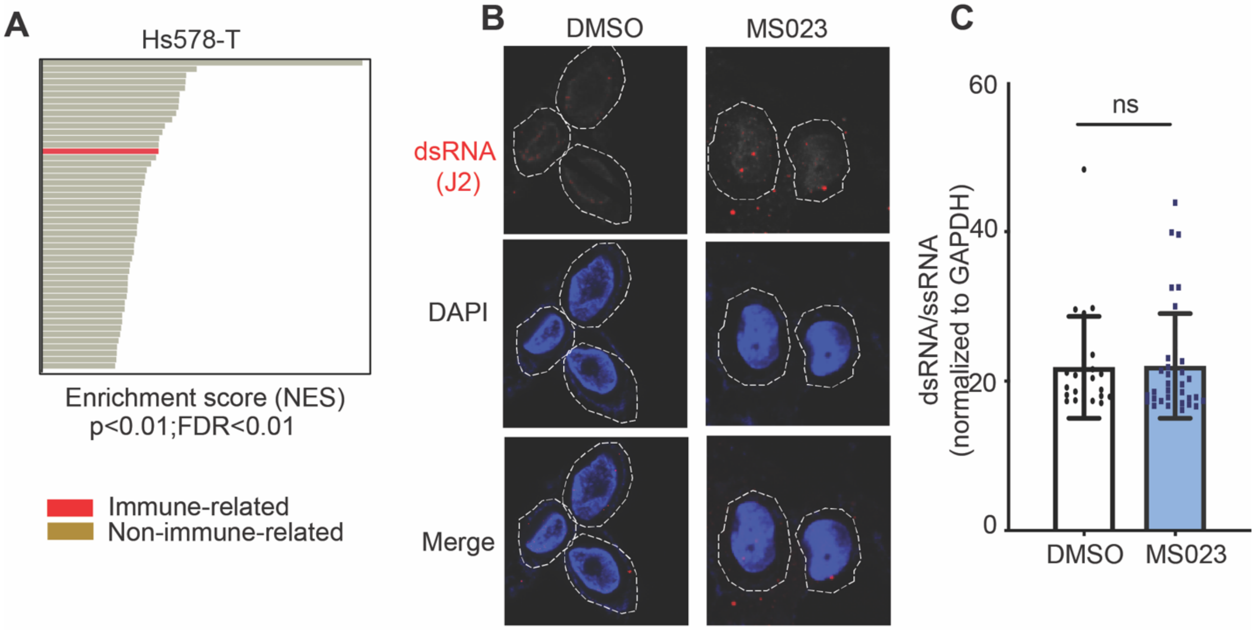
	AAC	TP53	SRSF1	SRSF2
MDA-MB-468	0.380697	🟨		
HCC1143	0.268349	🟨	🟨	
MDA-MB-436	0.248347	🟦		
CAL85-1	0.158293	🟨		
MDA-MB-231	0.122944	🟨		
HCC1395	0.10625	🟨		
HCC38	0.086839	🟨		
HCC1806	0.04663	🟦		
Hs-578-T	0.044544	🟨		
BT-549	0	🟨		
CAL-120	0	🟧		
MDAMB 157	0			

🟨 missense-mutation 🟦 frameshift 🟧 splice site

Supplementary Figure 1. **(A)** Growth curves of 17 TNBC cell lines with indicated concentrations of MS023 treatment for 5 days. **(B)** Correlation between area above curve (AAC) for MS023 and MTAP mRNA expression for 17 TNBC cell lines. **(C)** Correlation of AAC and common gene mutations for 13 TNBC cell lines. Genetic alteration data downloaded from CCLE database (https://portals.broadinstitute.org/ccle). **(D)** GSEA of the apoptosis pathway after MS023 treatment.



Supplementary Figure 2. **(A)** Flow cytometry cell cycle analysis for MDA-MB-468 cells cultured with or without MS023 for 72h. Data shown are mean ± s.d. of n = 3 independent assays. A one-way ANOVA was used to derive the p values. ***p<0.001, ****p<0.0001; n.s means not significant. **(B)** Apoptotic cell counts of MS023 treated for 3 days by caspase 3/7 staining. Data shown are mean ± s.d. of n = 3 independent experiments. A one-way ANOVA was used to derive the p values. ***p<0.001; n.s means not significant. **(C)** GSEA analysis for gene sets associated with interferon responses in MDA-MB-468 cell line following MS023 treatmwnt. **(D)** Volcano plot of log2 fold change for genes significantly upregulated (red in the right panel) or downregulated (blue in left panel) upon MS023 treatment (n=3) in Hs578-T cell line. **(E)** Gene set enrichment analysis (GSEA) of all ranked differentially expressed genes in Hs578-T after MS023 treatment.



Supplementary Figure 3. **(A)** Scatterplot of upregulated gene sets enriched in Hs578-T cell after MS023 treatment. Gene sets associated with immune response are red. **(B)** Cellular dsRNA was evaluated with anti-dsRNA (J2) immunofluorescence. **(C)** Quantification of cytoplasmic dsRNA signal intensity.