

## Preclinical evaluation of PRC2-targeting agents in NPC

**Table S1.** Patient characteristics

Characteristics	No. of patients	%
Total number of patients	93	
Age		
≤ 50	48	51.6
> 50	45	48.4
Gender		
Males	74	79.6
Females	19	20.4
Primary tumor (T) stage		
T1	18	19.4
T2	28	30.1
T3	31	33.3
T4	15	16.1
Unknown	1	1.1
Regional lymph nodes (N) stage		
N0	21	22.6
N1	34	36.6
N2	24	25.8
N3	13	14.0
Unknown	1	1.1
Metastatic disease		
M0	87	93.6
M1	6	6.5
Overall stage		
Stage I	2	2.2
Stage II	26	28.0
Stage III	40	43.0
Stage IVA	18	19.4
Stage IVB	4	4.3
Stage IVC	1	1.1
Unknown	2	2.2
Prior Chemotherapy		
No	10	10.8
Yes	47	50.5
Unknown	36	38.7
Prior Radiotherapy		
No	29	31.2
Yes	28	30.1
Unknown	36	38.7

## Preclinical evaluation of PRC2-targeting agents in NPC

**Table S2.** Clinical outcome of the 93 patients with archival NPC tumors analyzed in this study

	Frequency	%
Status		
Alive	52	55.9
Died of NPC	27	29.0
Died after protocol treatment complication	8	8.6
Died of other chemotherapy treatment complication	2	2.2
Died of concurrent illness	2	2.2
Died of other causes	2	2.2
Progression		
Without progression	64	68.8
Local failure	15	16.1
Regional failure	5	5.4
Distant failure	17	18.3

Note: 3 cases have both local-regional failure and distant failure. 29 cases have distant or local-regional failure.

**Table S3.** Survival analysis of EZH2, EED, SUZ12 and H3K27me3

	Hazard Ratio (HR)	95% CI	P value
OS			
EZH2 expression level	0.803	0.381-1.695	0.565
SUZ12 expression level	0.815	0.387-1.718	0.591
EED expression level	0.902	0.319-2.552	0.846
Primary tumor (T) stage	0.372	0.186-0.741	0.005
Regional lymph nodes (N) stage	0.409	0.215-0.776	0.006
Overall stage	0.278	0.115-0.672	0.004
PFS			
EZH2 expression level	0.812	0.399-1.652	0.566
SUZ12 expression level	0.838	0.413-1.701	0.624
EED expression level	0.787	0.280-2.209	0.649
Primary tumor (T) stage	0.529	0.282-0.990	0.047
Regional lymph nodes (N) stage	0.425	0.231-0.781	0.006
Overall stage	3.310	1.454-7.535	0.004
DMFS			
EZH2 expression level	1.321	0.431-4.052	0.626
SUZ12 expression level	0.849	0.277-2.605	0.775
EED expression level	0.429	0.057-3.233	0.411
LRFS			
EZH2 expression level	0.703	0.285-1.733	0.444
SUZ12 expression level	0.707	0.287-1.737	0.449
EED expression level	0.573	0.135-2.421	0.448

Note: 0 and +1 were classified as negative group; +2 and +3 were classified as positive group.

## Preclinical evaluation of PRC2-targeting agents in NPC

**Table S4.** Correlation of markers with NPC stage

	EZH2		P value
	Negative	Positive	
Distant-metastatic stage			1.000
Without Metastatic	25	62	
Metastatic	1	5	
Primary tumor (T)			0.021
T1 + T2	8	38	
T3 + T4	18	28	
Overall stage			0.121
Stage I + Stage II	5	24	
Stage III + Stage IV	21	43	
Local failure			0.771
Without local failure	22	54	
Local failure	4	13	
	SUZ12		P value
	Negative	Positive	
Distant-metastatic stage			1.000
Without Metastatic	23	64	
Metastatic	1	5	
Primary tumor (T)			0.058
T1 + T2	8	38	
T3 + T4	16	30	
Overall stage			0.204
Stage I + Stage II	5	24	
Stage III + Stage IV	19	45	
Local Failure			1.000
Without local failure	20	56	
Local failure	4	13	
	EED		P value
	Negative	Positive	
Metastatic stage			0.541
Without Metastatic	10	77	
Metastatic	1	5	
Primary tumor (T)			0.197
T1 + T2	3	43	
T3 + T4	8	38	
Overall stage			0.163
Stage II	1	28	
Stage III + Stage IV	10	54	
Local Failure			0.682
Without local failure	10	66	
Local failure	1	16	
	H3K27me3		P value
	Negative	Positive	
Metastatic stage			1.000
Without Metastatic	23	64	
Metastatic	1	5	
Primary tumor (T)			0.342
T1 + T2	10	36	

## Preclinical evaluation of PRC2-targeting agents in NPC

T3 + T4	14	32	
Overall stage			0.448
Stage II	6	23	
Stage III + Stage IV	18	46	
Local Failure			0.707
Without local failure	19	57	
Local failure	5	12	

**Table S5.** Frequency table of prognostic markers

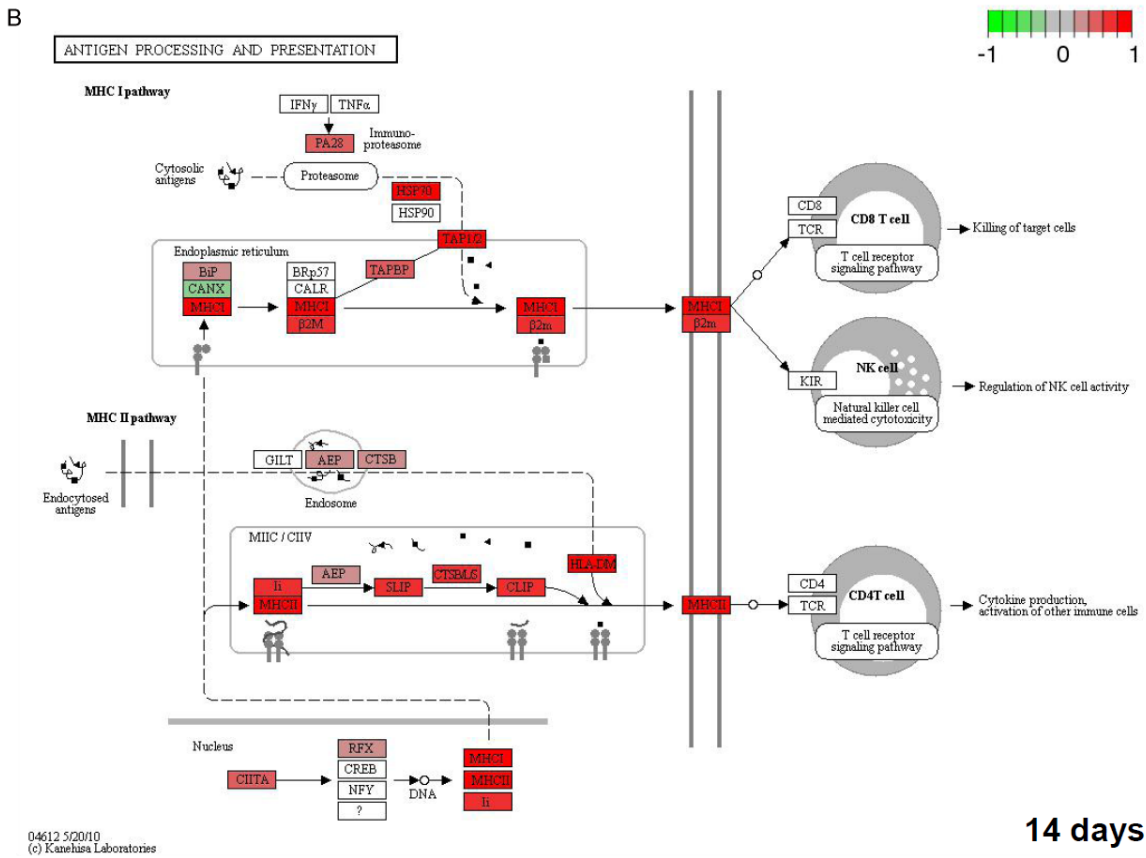
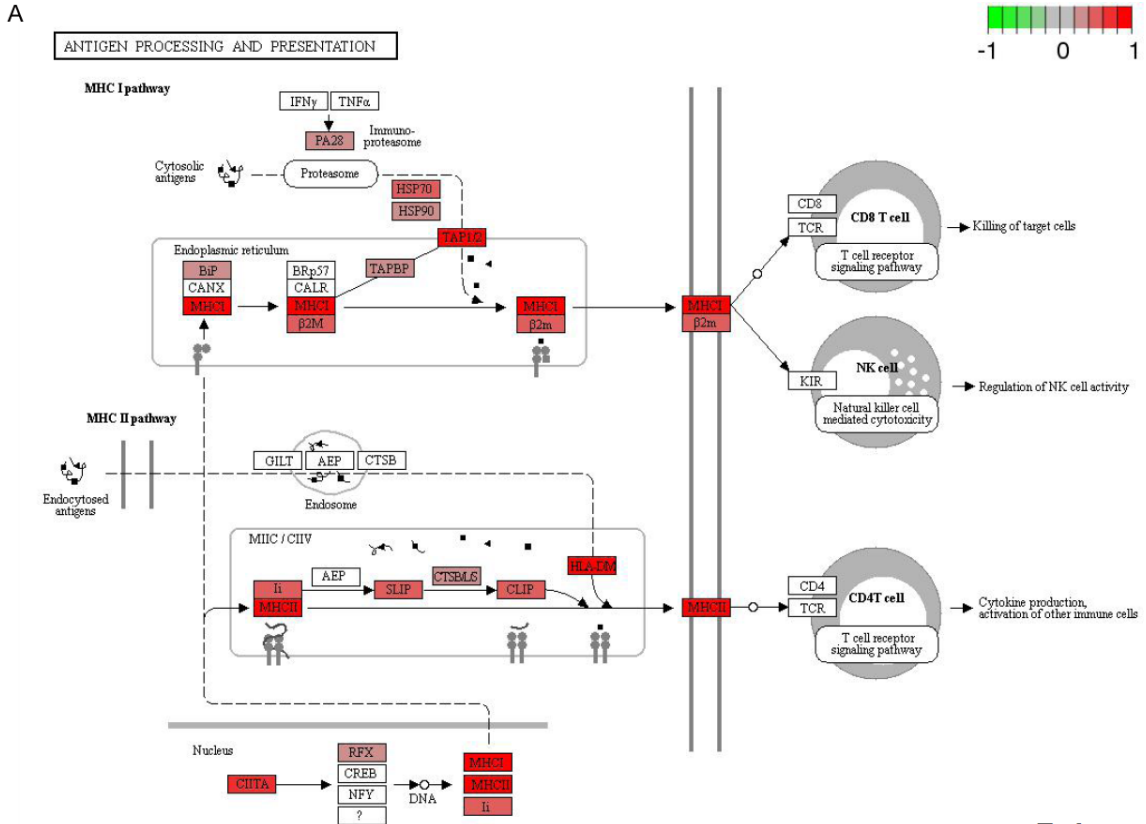
Prognostic marker	No. of patients	%
<b>EZH2</b>		
0 = none	11	11.83
+1 = weak	15	16.13
+2 = moderate	22	23.66
+3 = strong	45	48.39
<b>SUZ12</b>		
0 = none	14	15.05
+1 = weak	10	10.75
+2 = moderate	27	29.03
+3 = strong	42	45.16
<b>EED</b>		
0 = none	3	3.23
+1 = weak	8	8.60
+2 = moderate	36	38.71
+3 = strong	46	49.46
<b>H3K27me3</b>		
0 = none	18	19.35
+1 = weak	6	6.45
+2 = moderate	20	21.51
+3 = strong	49	52.69

**Table S6.** Spearman correlation analysis result among 4 biomarkers

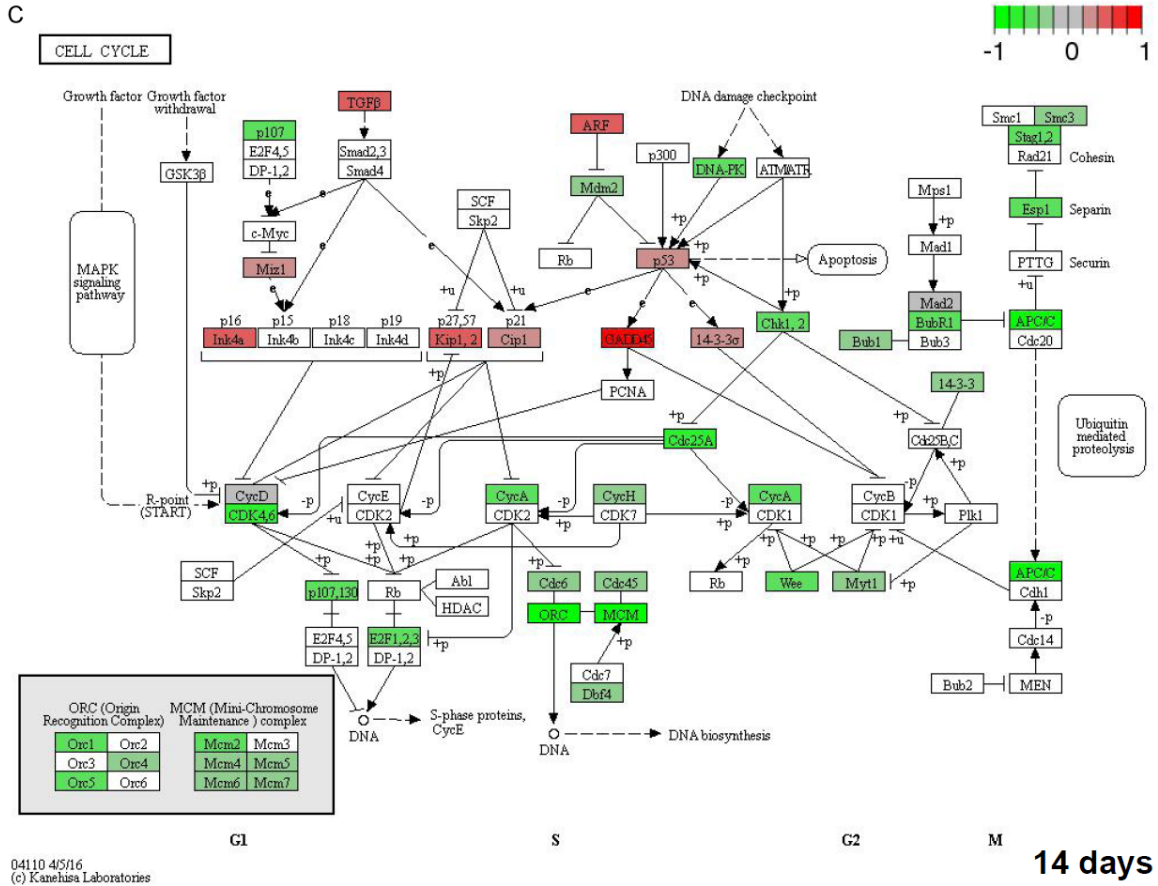
	EZH2	SUZ12	EED	H3K27me3
EZH2	/	0.476**	0.263*	0.409**
SUZ12	0.476**	/	0.256*	0.191
EED	0.263*	0.256*	/	0.225*
H3K27me3	0.409**	0.191	0.225*	/

Note: Table shows r values. \*means P < 0.05; \*\*means P < 0.000.

# Preclinical evaluation of PRC2-targeting agents in NPC



Preclinical evaluation of PRC2-targeting agents in NPC



**Figure S1.** KEGG pathway enrichment analysis. KEGG analysis of antigen processing and presentation pathway (ID: hsa04612) at 7 (A) and 14 (B) day. *MHC-1*, *TAP1/2*, *B2M*, *MHC-II*, *HLA-DM*, *HSP70*, *SLIP* and *CLIP* are red indicated those genes were up regulated after the treatment of EED226. (C) KEGG analysis of cell cycle (ID: hsa04110) at 14 days. *CDK4/6* are green indicated those genes were down regulated after the treatment of EED226.