

Efficacy and biomarkers of CAN017 in ESCC

Table S1. Summary of the efficacy of CAN017, HER3 and NRG1 expressions on PDX models of cohort 1

PDX model ID	TGI (%)	HER3 IHC score	NRG1 IHC score	HER3 RNAseq (log ₂ (FPKM+1))	NRG1 RNAseq (log ₂ (FPKM+1))
ES0214	135.11	3+	1+	5.97	2.98
ES0191	116.56	1+	2+	6.21	1.54
ES0042	109.43	1+	2+	4.16	3.68
ES0199	105.92	3+	3+	5.14	3.35
ES0147	100.62	2+	3+	7.17	2.3
ES0176	79.63	1+	2+	5.06	2.98
ES0190	78.42	1+	2+	4.93	3.37
ES0141	74.35	1+	1+	3.93	2.88
ES0189	60.26	1+	3+	5.74	-0.53
ES2411	45.06	1+	1+	4.9	1.2
ES0195	44.86	3+	1+	5.08	1.84
ES0172	44.58	2+	1+	5.14	1.14
ES0218	25.23	2+	1+	3.17	0.17
ES0201	24.05	1+	3+	5.73	1.72
ES0219	23.67	1+	1+	5.84	0.35
ES2267	16.09	1+	2+	7.98	-2
ES6824	14.61	1+	1+	5.26	-1.85
ES0148	13.13	0	3+	6.42	-2
ES0026	6.78	1+	2+	3.54	2.52
ES2263	0.57	2+	2+	1.44	3.55
ES0215	-2.04	1+	2+	-0.42	-0.72
ES0630	-6.04	0	1+	3.54	0.78
ES0204	-16.49	1+	1+	5.32	0.3
ES0136	-40.48	1+	1+	5.56	-1.12

Table S2. Summary of NRG1 expressions evaluated by RT-PCR on 11 NRG1-high and 13 NRG1-low PDX models of cohort 1

Groups	PDX model ID	ΔC _t (NRG1)
NRG1-high	ES0214	4.05848333
	ES2263	4.536124333
	ES0176	5.505088333
	ES0141	5.618715
	ES0191	5.837773667
	ES0199	6.643713333
	ES0147	6.866417
	ES0195	6.874196
	ES0042	6.914877333
	ES0172	7.077805333
	ES0190	7.426407667
NRG1-low	ES0630	8.162932333
	ES0026	8.552053
	ES0201	9.356858333
	ES0219	9.935386333
	ES0204	10.724936

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ES0189	10.98290967
ES0215	11.179748
ES0218	11.378266
ES0136	12.225814
ES6824	13.306448
ES2411	14.76201567
ES2267	16.686158
ES0148	17.12613767

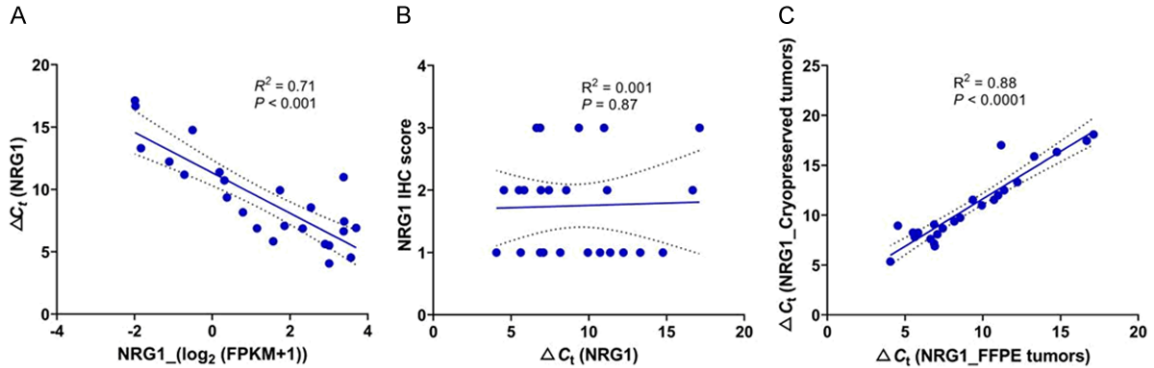


Figure S1. NRG1 expressions in tumor samples prior to treatment in cohort 1. A. Pearson correlation plots of the NRG1 mRNA expression detected by RNAseq and RT-PCR in PDX tumors (n = 24). B. Pearson correlation of the NRG1 mRNA and protein expressions in FFPE tumors (n = 24). C. Pearson correlation of the NRG1 mRNA expression in cryopreserved tumors and paired FFPE tumors. The linear regression was shown by a solid line, and 95% confidence interval (CI) of the values fitted by linear regression was shown by dark dotted lines. R², the coefficient of determination.

Table S3. The data of AUC curves for analyzing the threshold of NRG1 ΔC_t

Positive if less than or equal to ^a	Sensitivity	1-Specificity	Yoden Index ^b
3.0585	0	0	0
4.2973	0.125	0	0.125
5.0206	0.125	0.063	0.062
5.5619	0.25	0.063	0.187
5.7282	0.375	0.063	0.312
6.2407	0.5	0.063	0.437
6.7551	0.625	0.063	0.562
6.8703	0.75	0.063	0.687
6.8945	0.75	0.125	0.625
6.9963	0.875	0.125	0.75
7.2521	0.875	0.188	0.687
7.7947	1	0.188	0.812
8.3575	1	0.25	0.75
8.9545	1	0.313	0.687
9.6461	1	0.375	0.625
10.3302	1	0.438	0.562
10.8539	1	0.5	0.5
11.0813	1	0.563	0.437
11.279	1	0.625	0.375

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11.802	1	0.688	0.312
12.7661	1	0.75	0.25
14.0342	1	0.813	0.187
15.7241	1	0.875	0.125
16.9061	1	0.938	0.062
18.1261	1	1	0

^aThe smallest cut-off value was the minimum observed test value minus 1, and the largest cut-off value was the maximum observed test value plus 1. All the other cut-off values were the averages of two consecutive ordered observed test values.

^bYoden Index = Sensitivity-(1-specificity). A threshold with the maximum Yoden index meant the optimal threshold (Shown in bold).

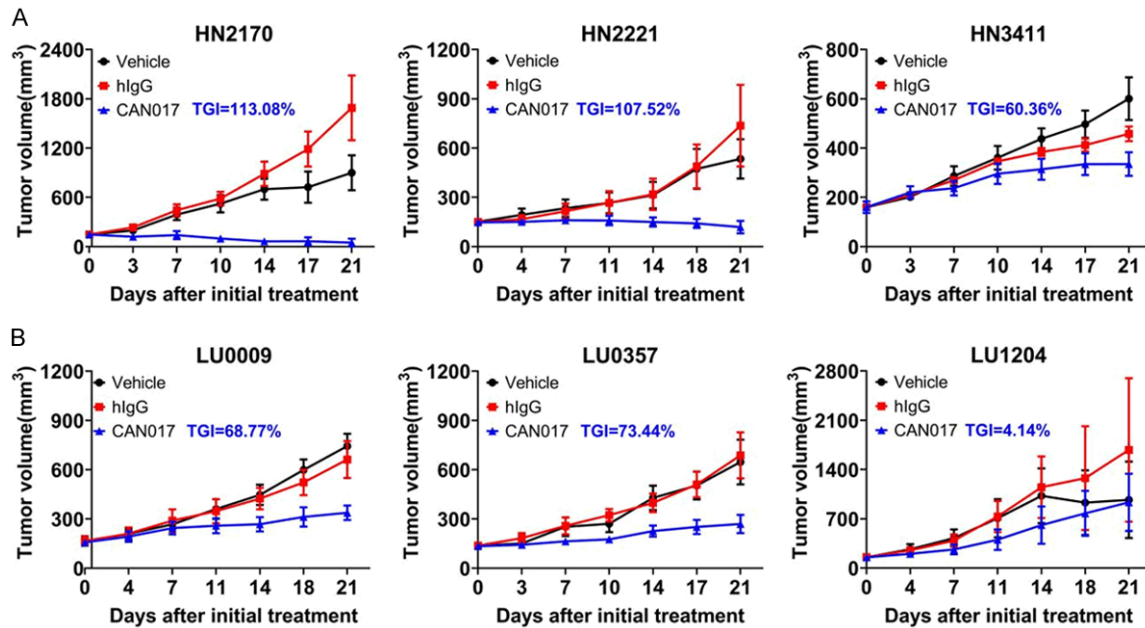


Figure S2. Efficacy of CAN017 on PDX models derived from head and neck cancer and NSCLC. A. Tumor growth curves showed the *in vivo* activity of CAN017 in 3 head and neck cancer PDX models. B. Tumor growth curves showed the *in vivo* activity of CAN017 in 3 NSCLC PDX models. Mice were randomized and treated with vehicle control, hlgG control (20 mg/kg) and CAN017 (20 mg/kg) when tumor volume reached approximately 150 mm³. The anti-tumor activity was depicted by TGI described in each picture. Data were presented as means \pm SDs.