Supplementary Materials

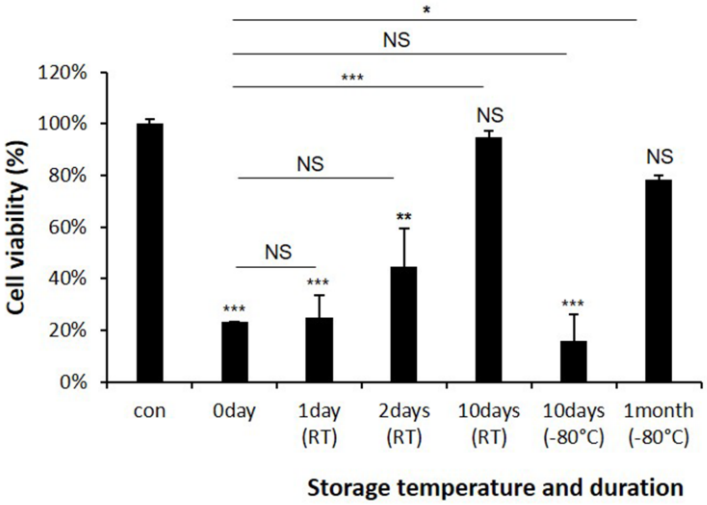

Figure S1. The effect of NTPAM according to storage temperature and duration. 2 h dose-NTPAM was stored at −80°C and room temperature (RT) for 0, 1, 2, 10 days or 1month. NTPAMs of various conditions were exposed to BCPAP cells for 24 h and cell viability was evaluated using the WST1 assay. Each figure is representative of three independent experiments. Results were analyzed using non-parametric one-way ANOVA followed by Dunnett's post-hoc test. Data were expressed as mean ± standard deviation of the mean (±SD). Differences were considered relevant at $p < 0.05$ (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

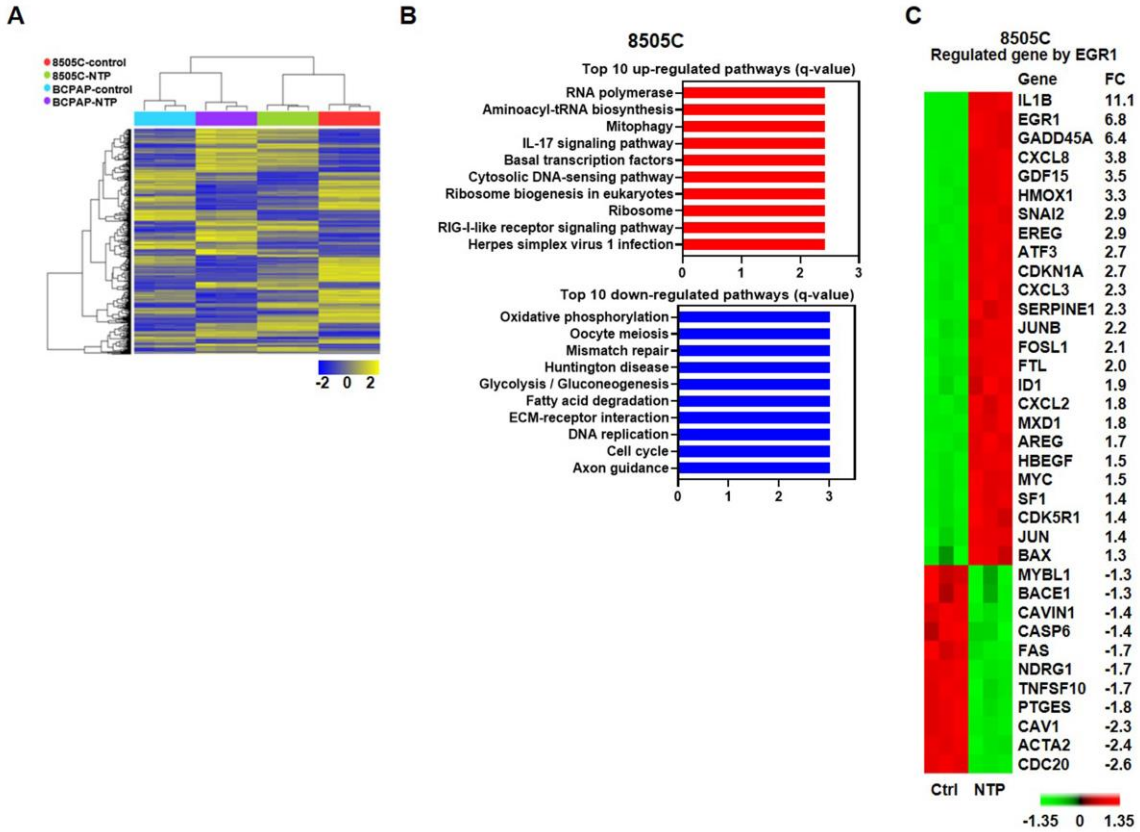

Figure S2. Transcriptomic analysis in thyroid cancer cells ± treatment with NTPAM. (A) Heatmap analysis of the significant changed genes with P value < 0.05 and Fold change > 2 comparing with or without NTPAM treatmend in BCPAP cells and 8505C cells (B) Top 10 up-regulated pathway and top 10 down-regulated pathways in 8505C cells in relation to NTPAM treatment. (C) Heatmap analysis of the significant changed genes related with EGR1 with P value < 0.05 comparing with or without NTPAM treatmend in 8505C cells.

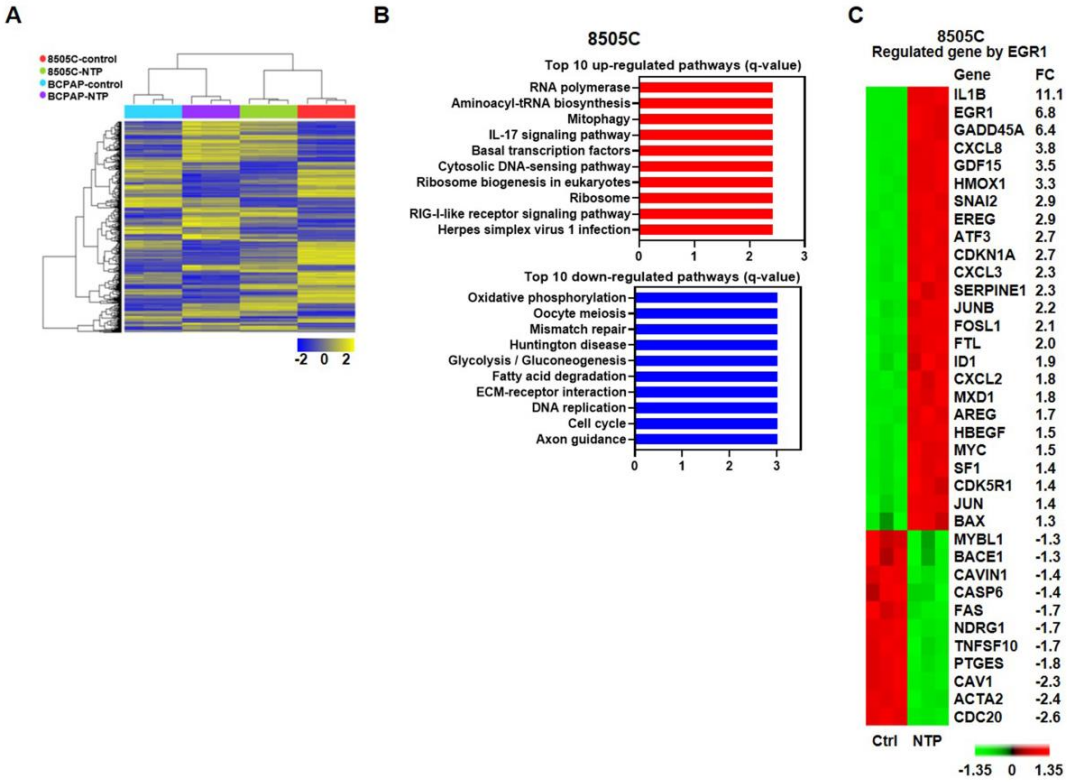

Figure S3. The effect of ATF4 in NTPAM-treated cell viability. BCPAP cells were transfected with or without ATF4-specific siRNA for 48 h, and then cells were treated with 2h dose-NTPAM for 24h. Cell viability was evaluated using the WST1 assay. Each figure is representative of three independent experiments. Results were analyzed using non-parametric one-way ANOVA followed by Dunnett's post-hoc test. Data were expressed as mean ± standard deviation of the mean (± SD). Differences were considered relevant at $p < 0.05$ (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

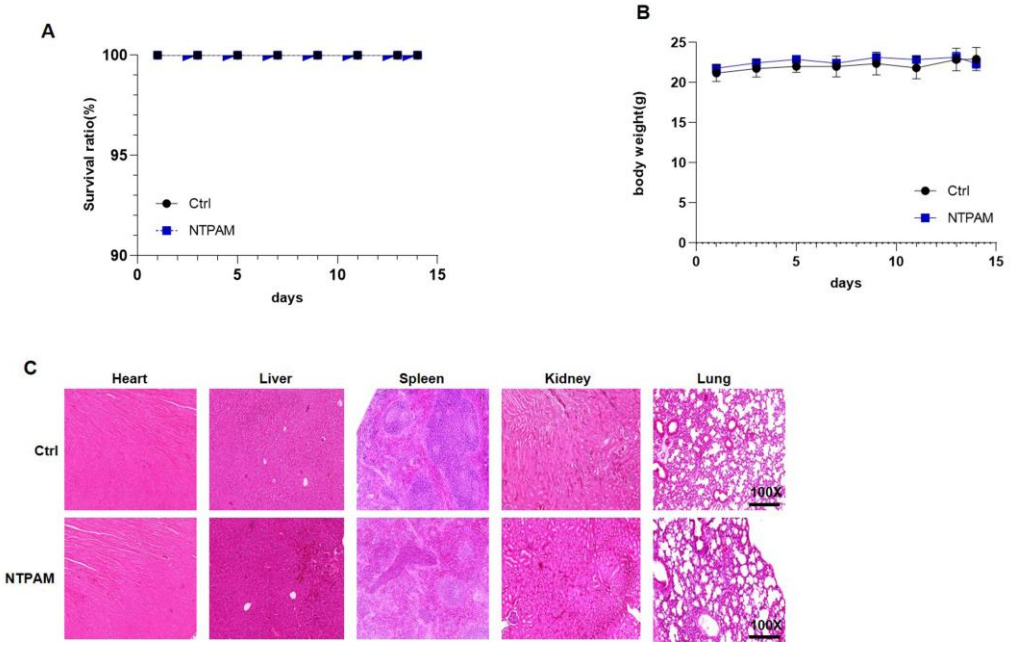

Figure S4. In vivo cytotoxic effect evaluation of NTPAM. 2 h dose-NTPAM was given to mice (C57BL/6 ,6weeks, 4mice) by introperitoneal injection (100μL) once daily for 2weeks. Survival ratio (A) and body weight (B) were monitored. C. Representative images (100X) of H&E staining of Major organs after the NTPAM treatments.

Table S1. Comparison of clinico-pathologic findings in relation to *EGR1* mRNA expression level in the THCA cohort.

Variables		Number of Patients	*EGR1* Expression		
			Low (N=250)	High (N=250)	*p* - Value
Age (years) (mean ± SD)			48.1±16.1	16.4±15.6	0.228
Gender (n, %)	Male	135	78(31.2)	57(22.8)	0.034*
	Female	365	172(68.8)	193(77.2)	
Tumor size, mm (mean ± SD)			1.65±1.19	1.30±1.04	0.014*
T stage (n, %)	T1-T2	308	162(64.8)	146(58.4)	0.141
	T3-T4	192	88(35.2)	104(41.6)	
Extrathyroidal extension (n, %)	No	348	164(65.6)	184(73.6)	0.056
	Minimal	134	73(29.2)	61(24.4)	
	Moderate/Advanced	18	13(5.2)	5(2.0)	
Lymph node metastasis (n, %)	No	277	124(49.6)	153(61.2)	0.009*
	N1a	151	91(36.4)	60(24.0)	
	N1b	72	35(14.0)	37(14.8)	
M stage (n, %)	M0	492	245(98.0)	247(98.8)	0.476
	M1	8	5(2.0)	3(1.2)	
Stage (n, %)	I	284	136(54.4)	148(59.2)	0.146
	II	52	21(8.4)	31(12.4)	
	III	111	63(25.2)	48(19.2)	
	IV	53	30(12.0)	23(9.2)	
$BRAF^{V600E}$ mutation (n, %)	No	254	119(47.6)	135(54.0)	0.288
	Yes	232	123(49.2)	109(43.6)	
	Fusion	9	4(1.6)	5(2.0)	
	Other mutation	5	4(1.6)	1(0.4)	

p values from unpaired *t*-tests for continuous parametric variables and the Mann–Whitney U-test for nonparametric variables. The chi-square test and Fisher's exact test were used to evaluate the significance of the correlations of EGR1 expression with clinical and pathological parameters.TNM classification from AJCC(American Joint Committee on Cancer) 7^{th} edition was used. * $p < 0.05$ between the two categories for a given variable.

Table S2. Multivariable regression analysis of EGR1 expression associated with the clinic-pathologicical parameters.

Factors		Exp(β)	SE	95.0% CI	*p*-Value
Tumor size > 2cm	Age	0.9	0.006	(0.980, 1.004)	0.183
	High EGR1	1.138	0.196	(0.775, 1.670)	0.510
	Low EGR1				
LN metastasis	Age	1.015	0.006	(1.004, 1.027)	0.010*
	High EGR1	0.604	0.183	(0.422, 0.865)	0.006*
	Low EGR1				

Multivariate logistic regression analysis was performed to calculate OR and 95% CI for each covariable. The final multivariate model was based upon a stepwise method for clinical factors associated with EGR1 expression in univariate models. * $P<0.05$ between the two categories for a given variable. SE, standard error, Exp(β); OR, odds ratio, CI; confidence interval.