Supplementary Materials

An *in situ* spontaneously-forming micelle-hydrogel system with programable release for sequential therapy of anaplastic thyroid cancer

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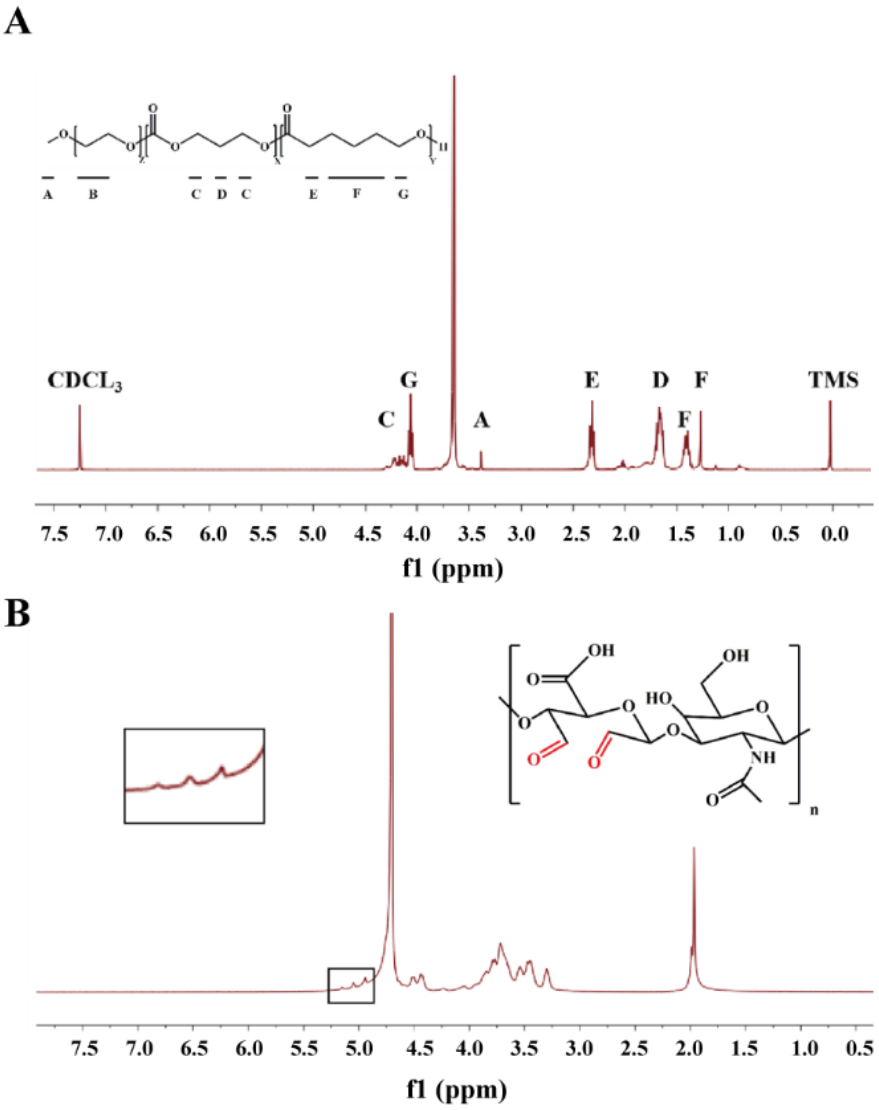
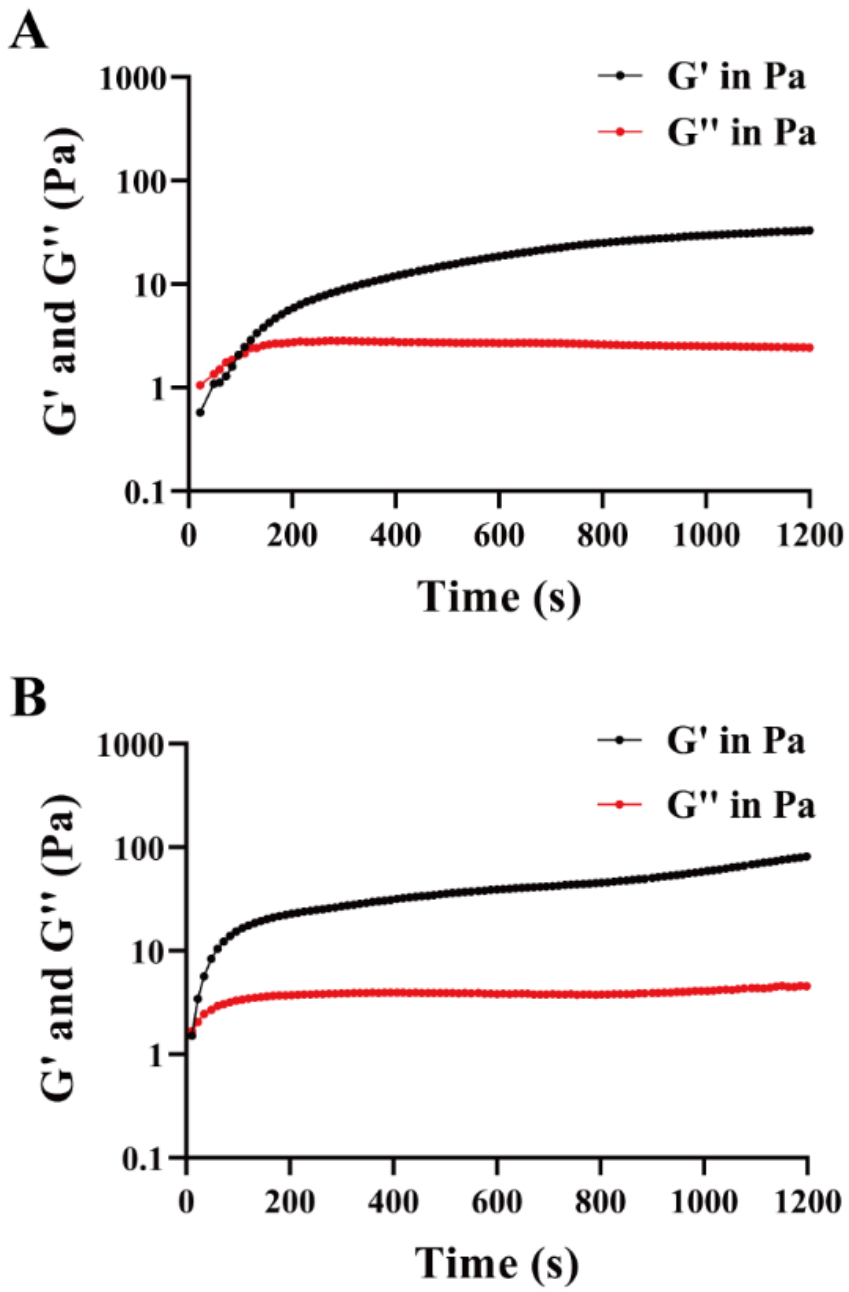
Supplementary Table 1. Characteristics of ATC cell lines C643 and 8305C

Cell Line	**C643**	**8305C**
Year of establishment	1987	1993
Patient Age	76	67
Patient Gender	Male	Male
Derivation	Primary Tumor	Primary Tumor
BRAF	-	p.V600*
HRAS	p.G13R*	-
TP53	p.R248Q	p.R273C
TERT promoter	c.-124C>T	c.-146C>T

* Key genetic driver.

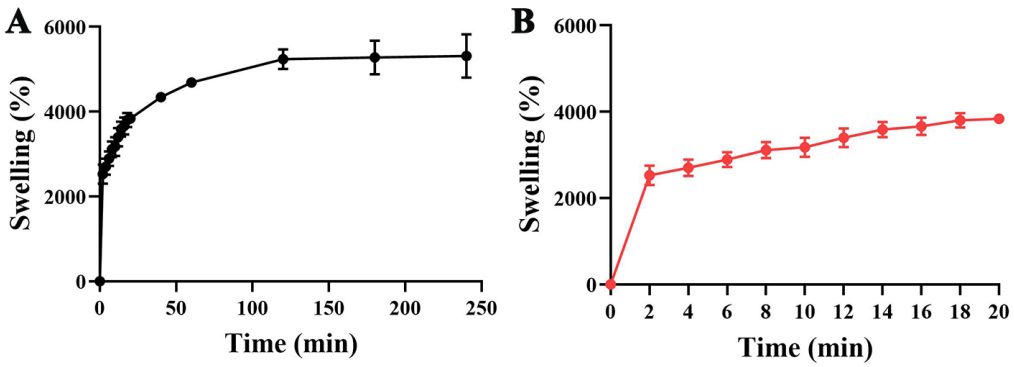


Supplementary Figure 1. ^{1}H**-NMR spectrum of MPEG–P(CL-*ran*-TMC) in $CDCl_3$ (A) and AHA (B).**

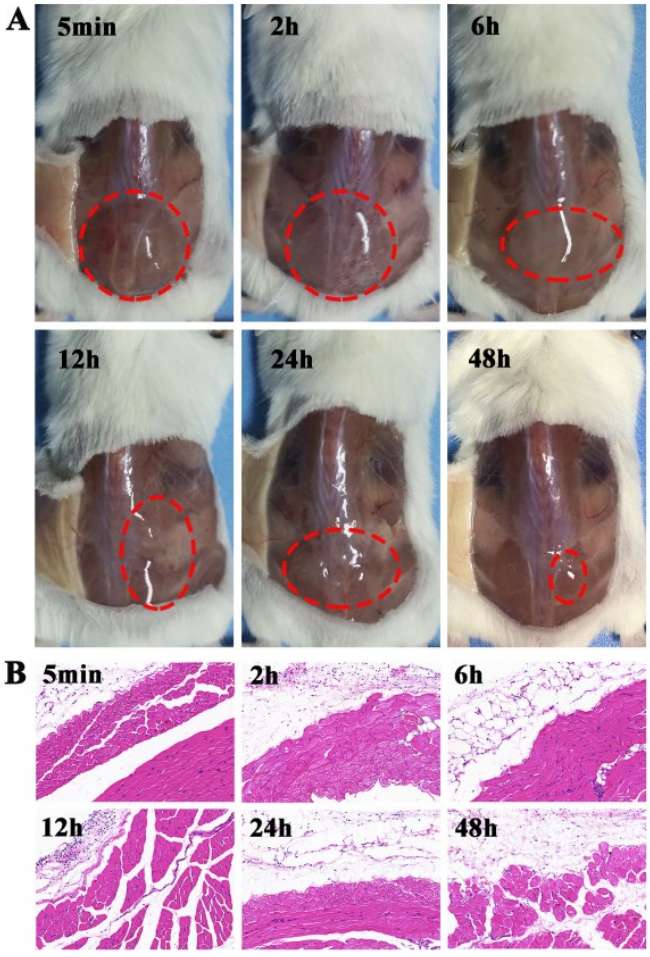


Supplementary Figure 2. Rheological analysis for the drug loaded NOCC/AHA hydrogel.

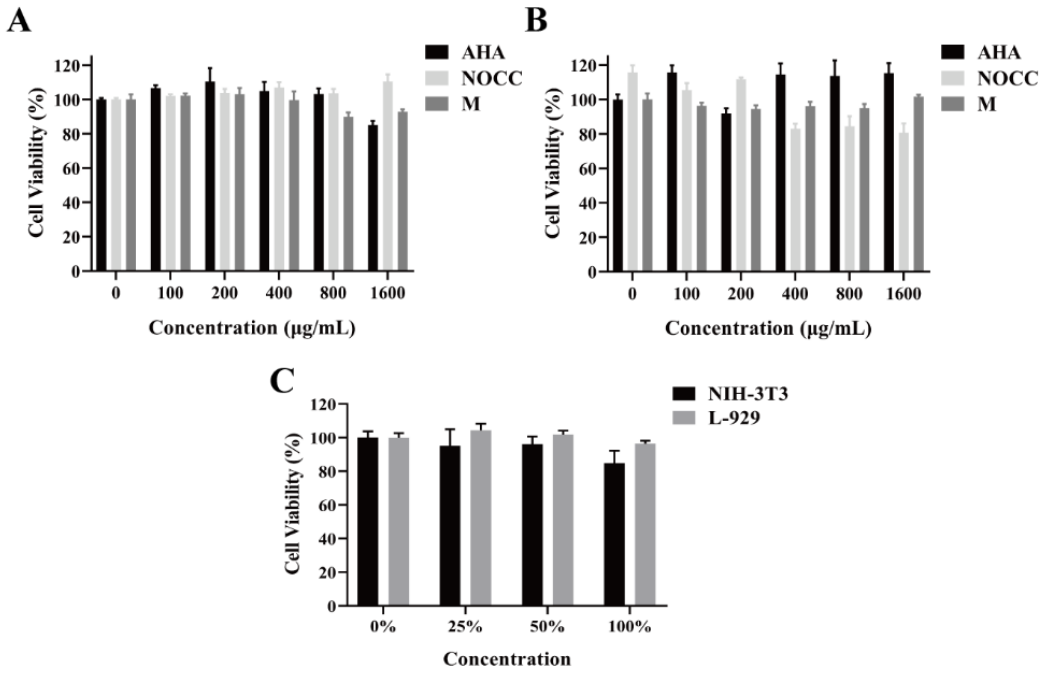
Time-dependence of storage modulus (G'), loss modulus (G'') for the drug loaded NOCC/AHA hydrogel. (A) DDP-hydrogel; (B) P_m-hydrogel.



Supplementary Figure 3. (A&B) Swelling kinetics of NOCC/AHA hydrogel in the different time.

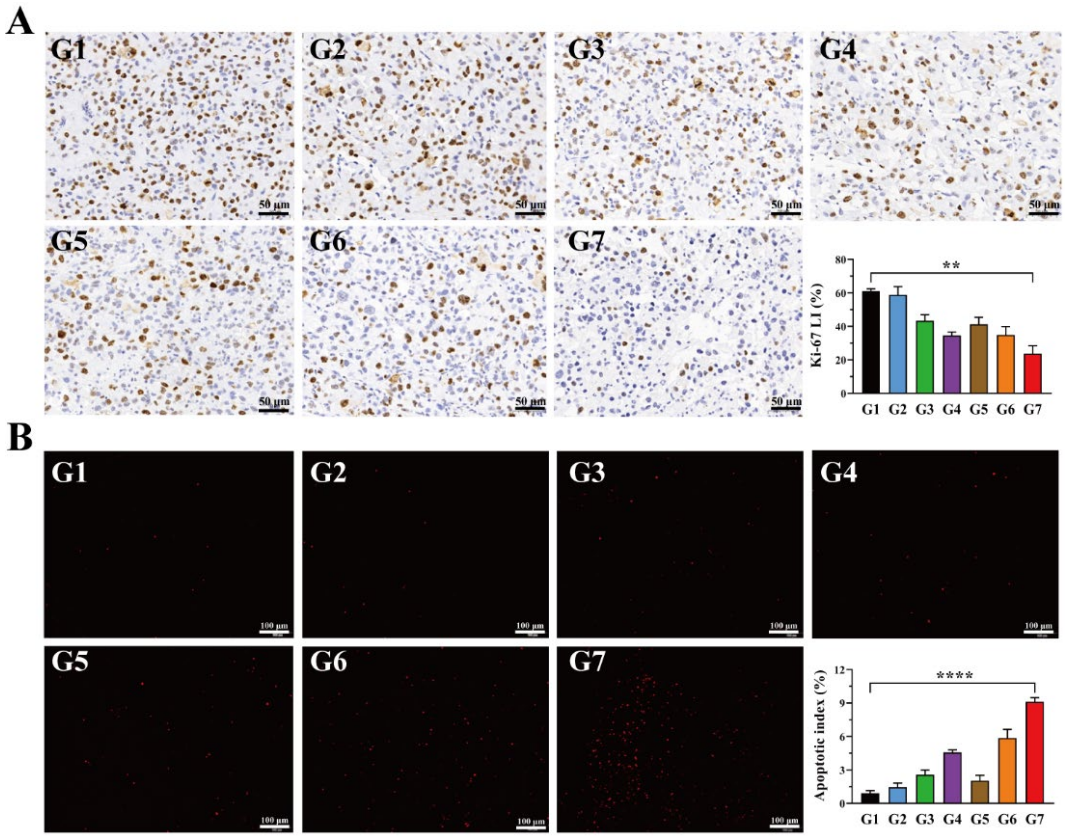


Supplementary Figure 4. *In vivo* degradation and biocompatibility of the NOCC-AHA hydrogel. (A) Gross observation of degradation assay in the different time; (B) Histological observations of biocompatibility assay in the different time.



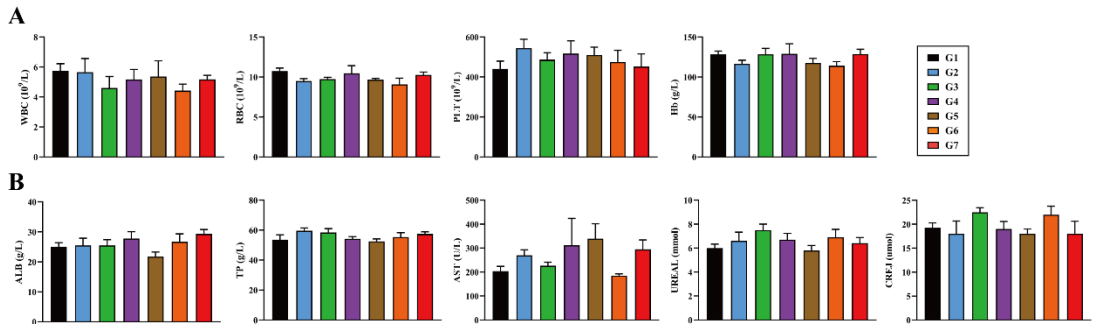
Supplementary Figure 5. Effect of AHA, NOCC, MPEG–P(CL-*ran*-TMC) and NOCC/AHA hydrogel extracts on cell viability measured by MTT assay.

(A) Cytotoxicity on NIH-3T3 and (B) L929 cells after 2-day incubation with AHA, NOCC or MPEG–P(CL-*ran*-TMC) at different concentrations; (C) Cytotoxicity on NIH-3T3 cells and L929 cells after 2-day incubation with the NOCC/AHA hydrogel extracts. Data were presented as mean ± SD (n = 3).



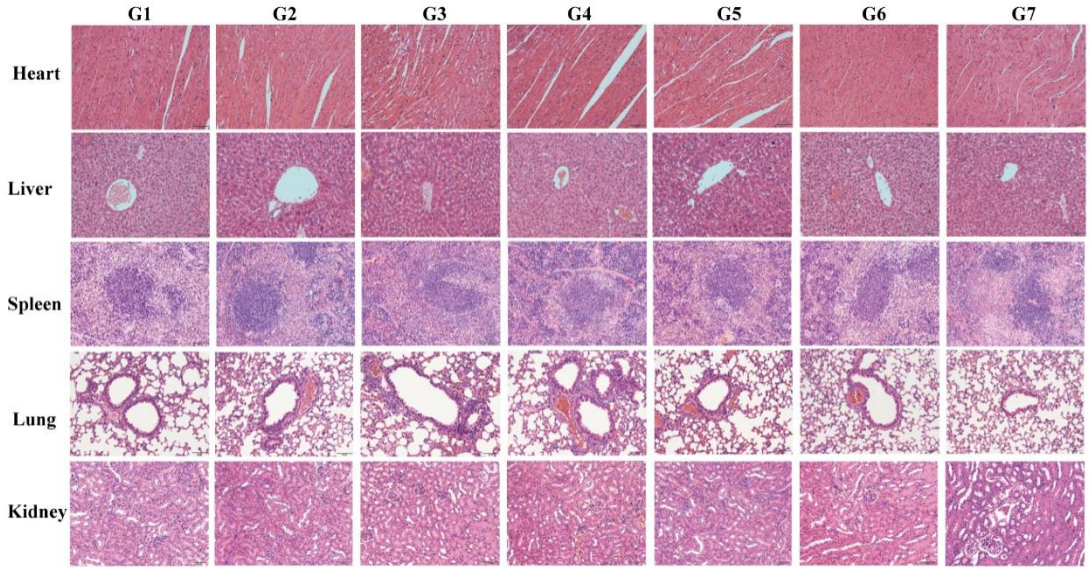
Supplementary Figure 6. Ki-67 immunohistochemical and TUNEL immunofluorescent staining of 8305C tumors.

(A) Representative Ki-67 immunohistochemical images of 8305C tumors and mean Ki-67 LI for each group (G1: NS i.t., G2: Micelle-hydrogel i.t., G3: P_m + DDP i.v., G4: P_m + DDP i.t., G5: P_m-hydrogel i.t., G6: DDP-hydrogel i.t., G7: iMHS i.t.). Scale bar = 50 μm; (B) Representative TUNEL immunofluorescent images of 8305C tumors and mean apoptotic index for each group. Scale bar = 100 μm. LI: labelling index.

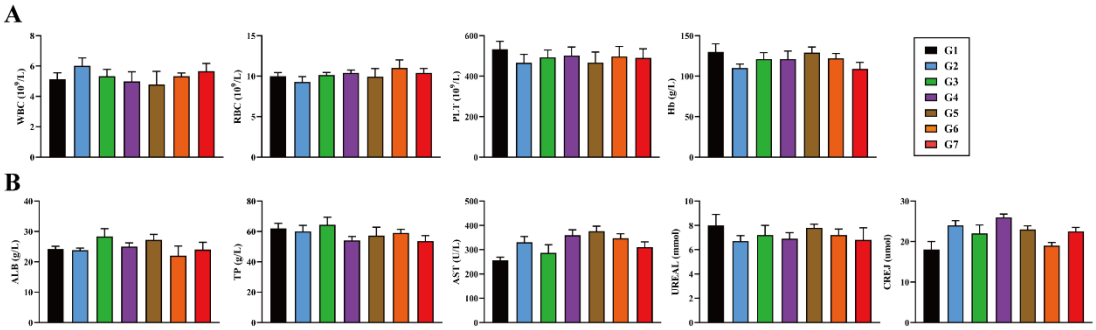


Supplementary Figure 7. Complete blood count and serum biochemistry study of the C643 subcutaneous tumor-bearing mice.

(A) Complete blood count including white blood cell (WBC), red blood cell (RBC), hemoglobin (Hb) and platelet (PLT) of each group; (B) Serum chemistry profile including total protein (TP), albumin (ALB), aspartate transaminase (AST), blood urea (UREAL), creatinine (CREJ) of each group.

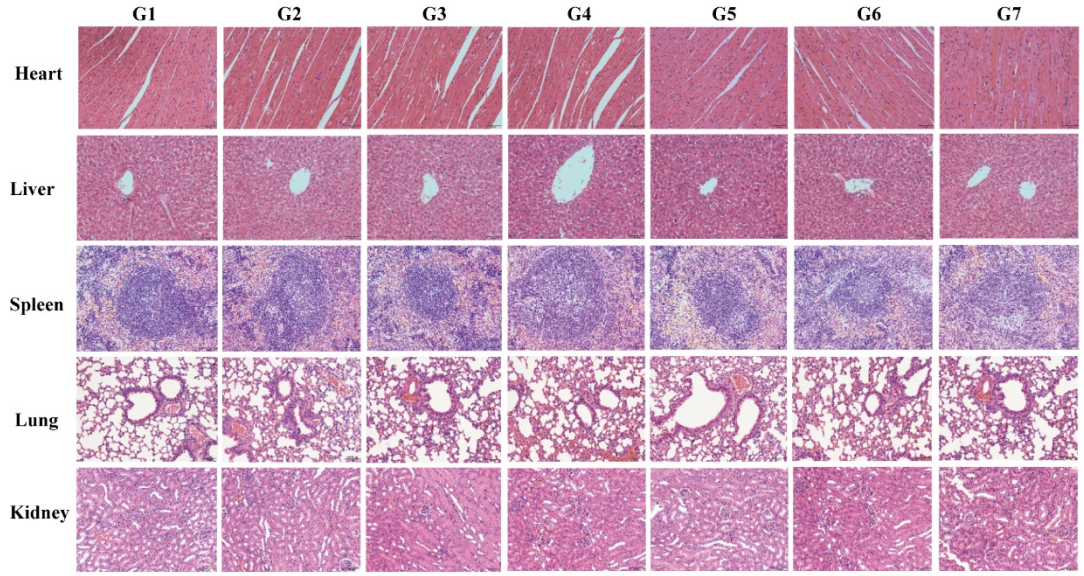


Supplementary Figure 8. Representative hematoxylin-eosin staining images of major organs (heart, lung, liver, spleen, and kidney) of each group in the C643 subcutaneous tumor-bearing mice.



Supplementary Figure 9. Complete blood count and serum biochemistry study of the 8305C subcutaneous tumor-bearing mice.

(A) Complete blood count including white blood cell (WBC), red blood cell (RBC), hemoglobin (Hb) and platelet (PLT) of each group; (B) Serum chemistry profile including total protein (TP), albumin (ALB), aspartate transaminase (AST), blood urea (UREAL), creatinine (CREJ) of each group.



Supplementary Figure 10. Representative hematoxylin-eosin staining images of major organs (heart, lung, liver, spleen, and kidney) of each group in the 8305C subcutaneous tumor-bearing mice.