

Supplementary Material

Sarcoma-Targeting Peptide-Decorated Polypeptide Nanogel Intracellularly Delivers Shikonin for Upregulated Osteosarcoma Necroptosis and Diminished Pulmonary Metastasis

Suoyuan Li^{1,4,#}, Tao Zhang^{1,#}, Weiguo Xu^{2,#}, Jianxun Ding^{2,✉}, Jing Xu³, Wei Sun¹, Hongsheng Wang³, Mengxiong Sun¹, Zhengdong Cai^{1,3,✉}, Yingqi Hua^{1,3,✉}

1. Department of Orthopedics, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200080, P. R. China

2. Key Laboratory of Polymer Ecomaterials, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, P. R. China

3. Shanghai Bone Tumor Institution, Shanghai 201620, P. R. China

4. Department of Orthopedics, Suzhou Municipal Hospital, Nanjing Medical University, Suzhou 215000, P. R. China

#These authors contributed equally to this work.

✉ Corresponding authors: Yingqi Hua, E-mail: yhua@shsmu.edu.cn; Jianxun Ding, E-mail: jxding@ciac.ac.cn; Zhengdong Cai, E-mail: czd856@vip.163.com.

Figure Legends

Scheme S1. Synthesis of mPEG-P(LP-co-LC).

Scheme S2. Synthesis pathway for NH₂-PEG-P(LP-co-LC).

Scheme S3. Synthesis process of STP-PEG-P(LP-co-LC).

Figure S1. ¹H NMR spectra of *t*-Boc-NH-PEG₁₁₃-P(LP₁₂-co-LC₄), NH₂-PEG₁₁₃-P(LP₁₂-co-LC₄), MI-PEG₁₁₃-P(LP₁₂-co-LC₄), STP, and STP-PEG₁₁₃-P(LP₁₂-co-LC₄).

Figure S2. FT-IR spectra of *t*-Boc-NH-PEG₁₁₃-P(LP₁₂-co-LC₄), NH₂-PEG₁₁₃-P(LP₁₂-co-LC₄), MI-PEG₁₁₃-P(LP₁₂-co-LC₄), STP, and STP-PEG₁₁₃-P(LP₁₂-co-LC₄).

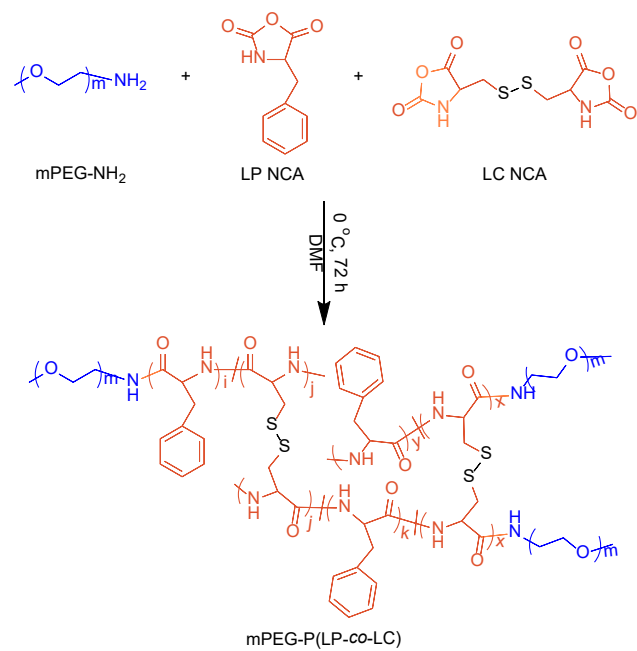
Figure S3. Binding of STP-FITC and vimentin antibody with peripheral white blood cells (WBCs). Human WBCs were incubated with STP-FITC, anti-VIM 488, and Isotype IgG 488, and analyzed by flow cytometry.

Figure S4. Cytotoxicity of STP-NG/SHK *in vitro*. Necroptosis in four groups in osteosarcoma 143B cells. Each set of data was represented as mean ± SEM ($n = 3$; $^*P < 0.001$).

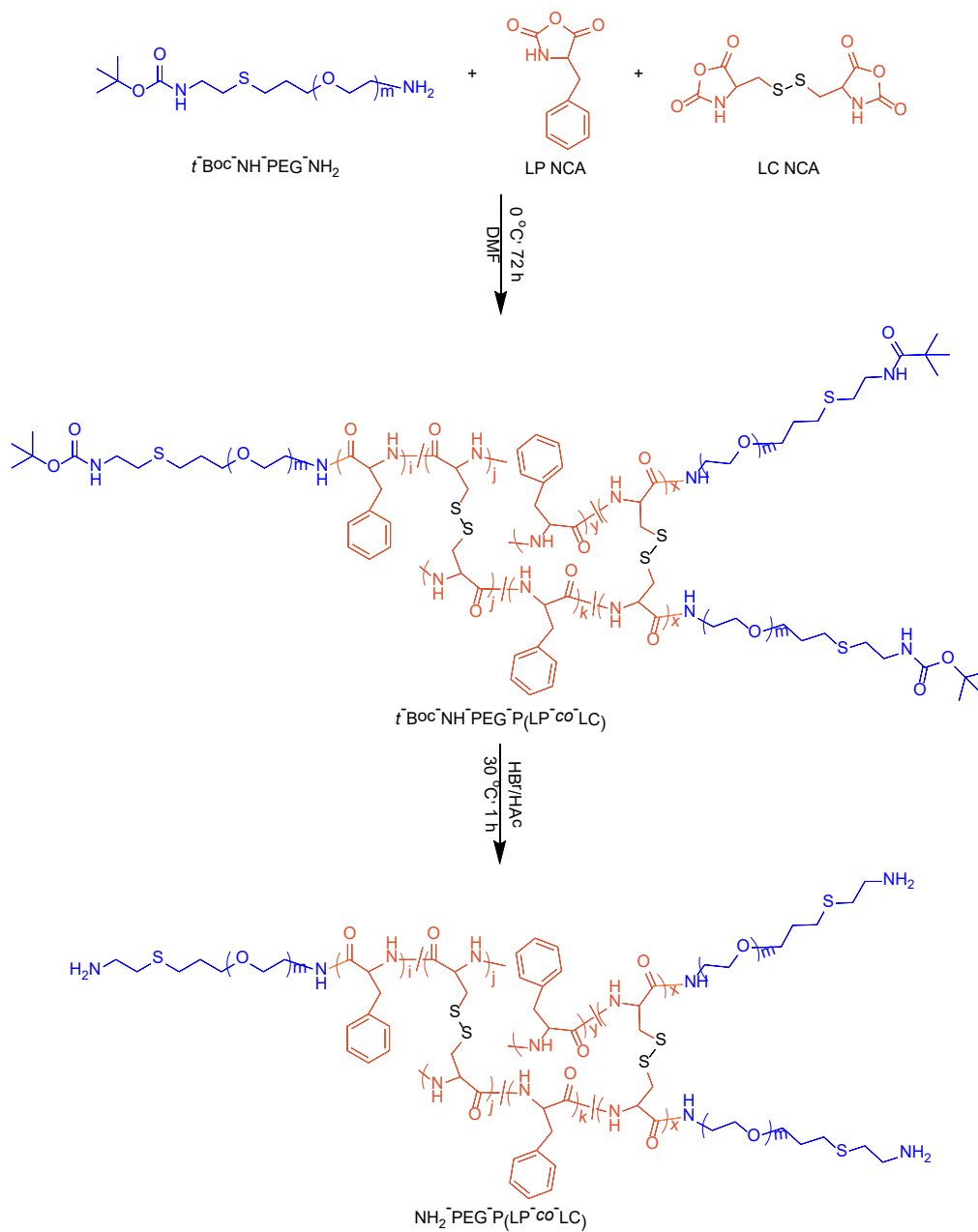
Figure S5. Effect of STP-NG/SHK on the cell cycle *in vitro*. Human osteosarcoma 143B cells in subG1, G0–G1, S, and G2–M states of the cell cycle were measured with propidium iodide (PI). SHK, NG/SHK or STP-NG/SHK treatment for 24 h did not change cell cycle status. Each set of data was represented as mean ± SEM ($n = 3$).

Figure S6. Pulmonary metastasis accounted for the proportion of total lung area. The proportion of area of pulmonary metastasis to the area of whole lung section was measured by Image-Pro Plus 6.0 software and calculated. Each set of data was represented as mean ± SEM ($n = 3$; $^*P < 0.001$).

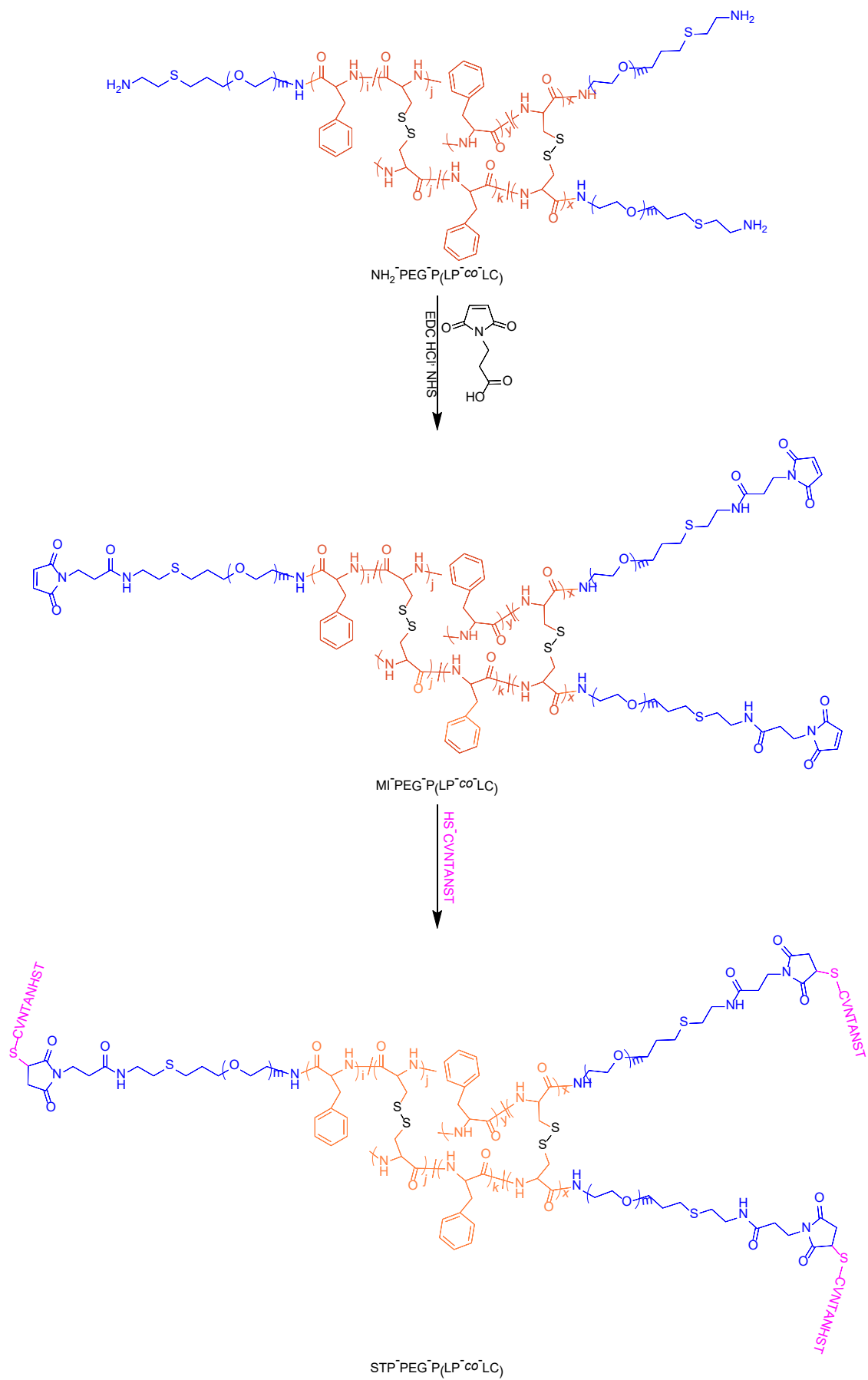
Figure S7. Toxicity of empty nanoparticle. (A) Cytotoxicity of empty nanoparticle toward 143B and hFOB1.19 cells. (B) The AST and ALT level of mice after treated with empty nanoparticle (*i.e.*, STP-NG). (C) Tumor volume and mice weight after treatment with empty nanoparticle. (D) Tumor weight, lung weight, and lung metastases counting were calculated.



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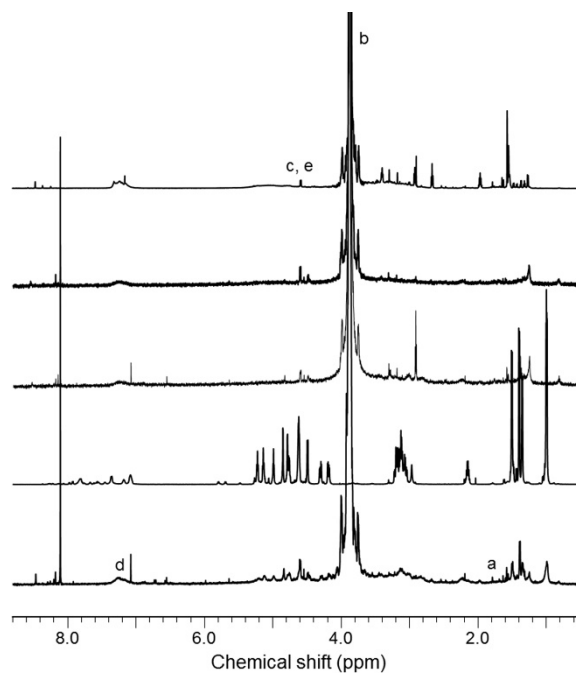
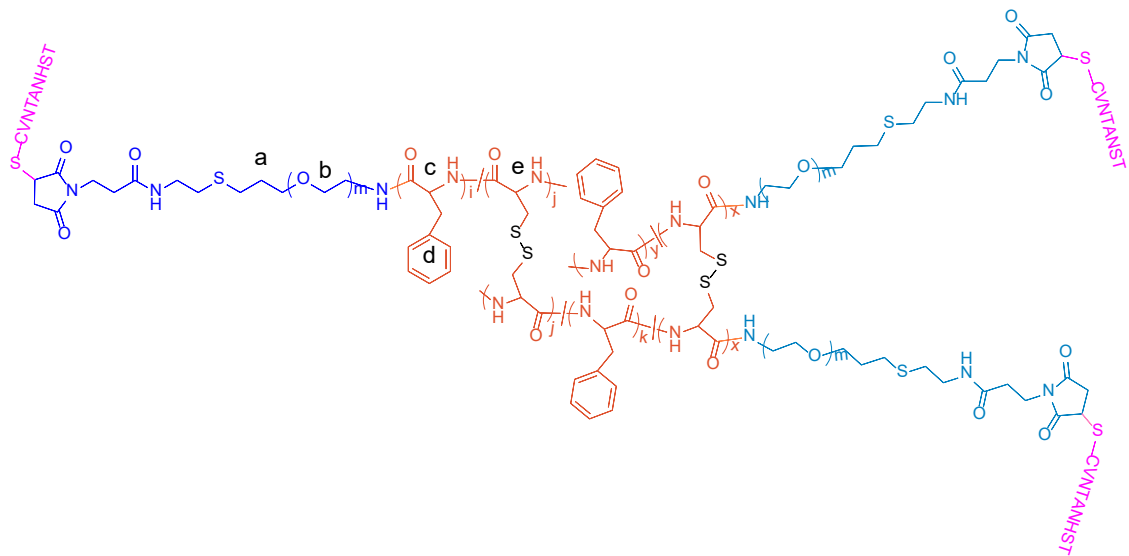


Figure S1. ^1H NMR spectra of $t\text{-Boc-NH-PEG}_{113}\text{-P}(\text{LP}_{12}\text{-co-LC}_4)$, $\text{NH}_2\text{-PEG}_{113}\text{-P}(\text{LP}_{12}\text{-co-LC}_4)$, $\text{MI-PEG}_{113}\text{-P}(\text{LP}_{12}\text{-co-LC}_4)$, STP , and $\text{STP-PEG}_{113}\text{-P}(\text{LP}_{12}\text{-co-LC}_4)$.

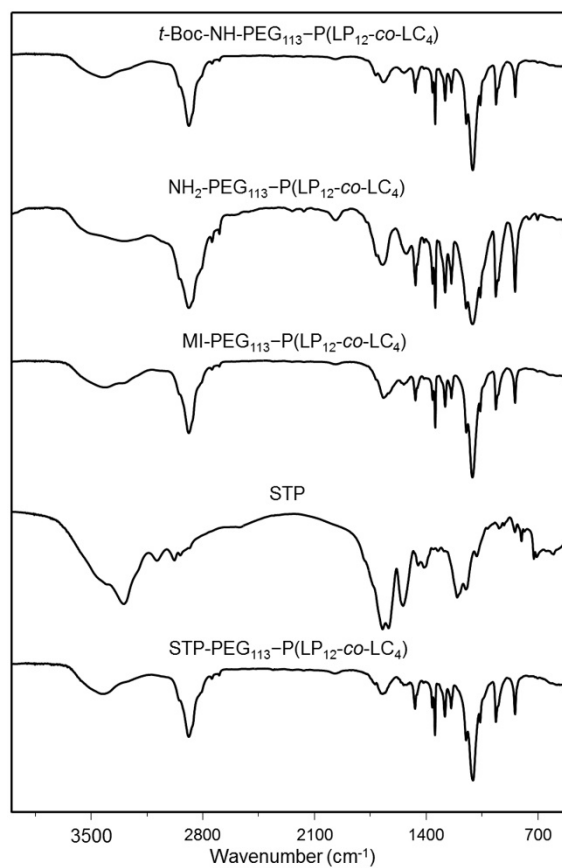


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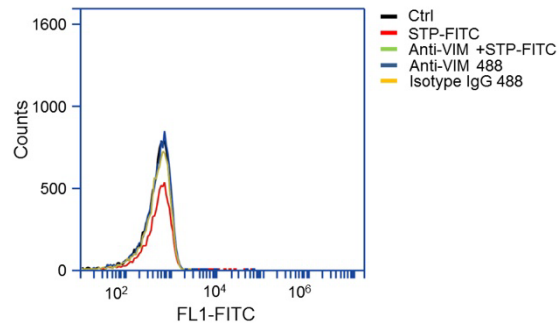


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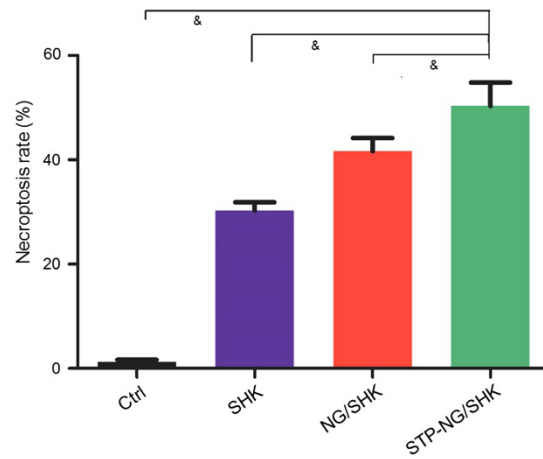


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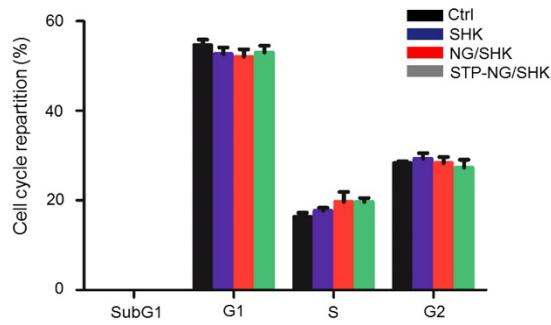


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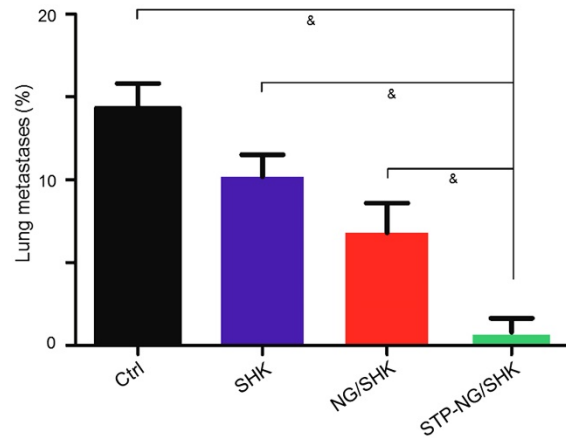


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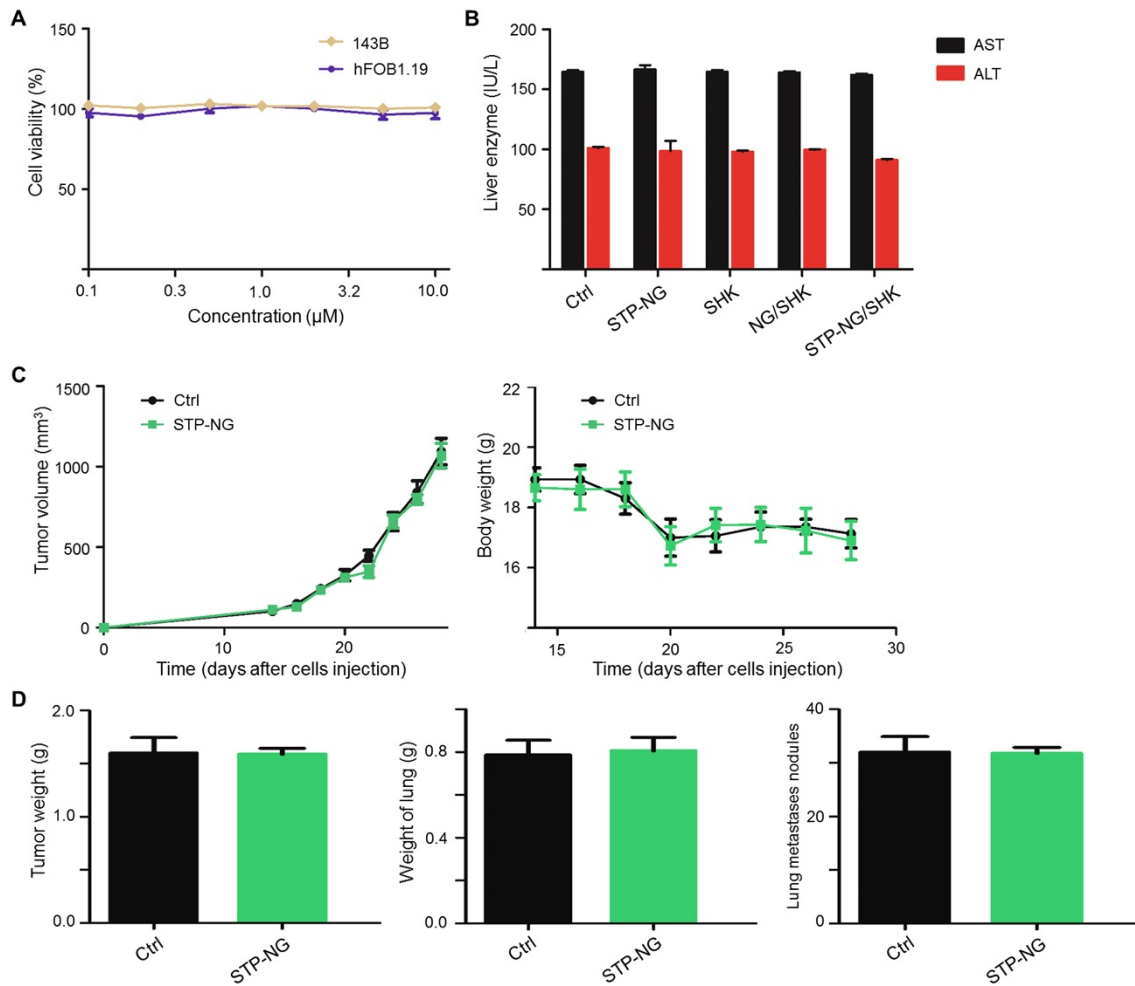


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