Supporting Information for:

Eliciting an Immune Hot Tumor Niche with Biomimetic Drug-based Multi-functional Nanohybrids Augments Immune Checkpoint Blockade-based Breast Cancer Therapy

Wei Du[1#], Chen Chen[1#], Peng Sun[2], Shengchang Zhang[1], Jing Zhang[1], Xiaoyu Zhang[1], Ying Liu[1], Rui Zhang[1], Chongzheng Yan[1], Changchun Fan[3], Jibiao Wu[4], Xinyi Jiang[1*]

[1]Department of Pharmaceutics, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, 44 Wenhuaxi Road, Jinan, Shandong Province 250012, PR China

[2]College of Pharmacy, Shandong University of Traditional Chinese Medicine, Jinan, China

[3]Shandong Provincial Qianfoshan Hospital, the First Hospital Affiliated with Shandong First Medical University, Jinan, Shandong 250014, PR China

[4]Laboratory of Traditional Chinese Medicine Classical Theory, Ministry of Education, Shandong University of Traditional Chinese Medicine, Jinan, China

[#] These authors contributed equally

[*] Corresponding author: Xinyi Jiang, Ph.D.

Phone/Fax: +86-0531-88382015

Email: xinyijiang@sdu.edu.cn

Table 1. Primer sequences

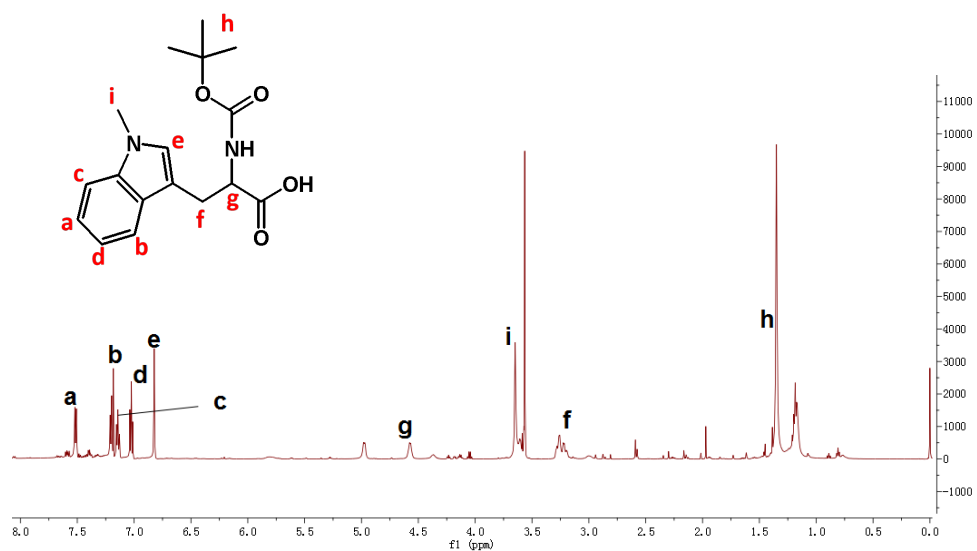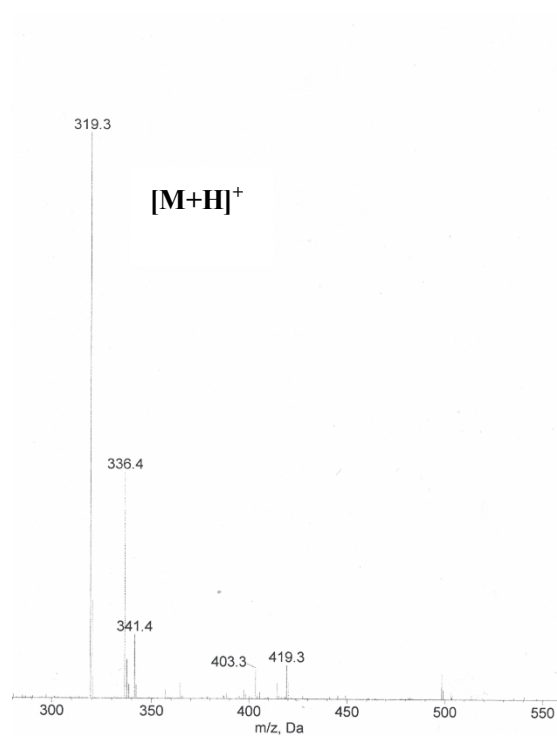| Genes	Primer sequence (5'-3')
NOS2	GAGACAGGGAAGTCTGAAGCAC
	CCAGCAGTAGTTGCTCCTCTTC
IL-12b	TTGAACTGGCGTTGGAAGCACG
	CCACCTGTGAGTTCTTCAAAGGC
Arg 1	CATTGGCTTGCGAGACGTAGAC
	GCTGAAGGTCTCTTCCATCACC
Tgfb	CCACCTGCAAGACCATCGAC
	CTGGCGAGCCTTAGTTTGGAC

Figure S1. The 1H-NMR spectrum of 1-MT-Boc.
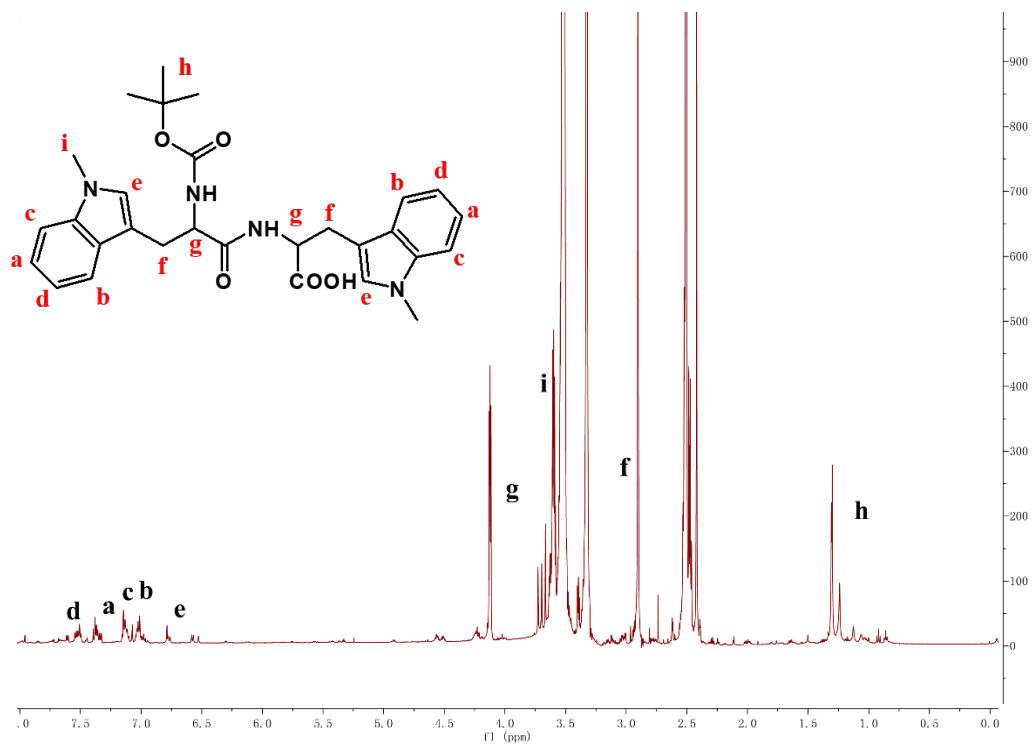

Figure S2. The ESI-MS spectrum of 1-MT-Boc.
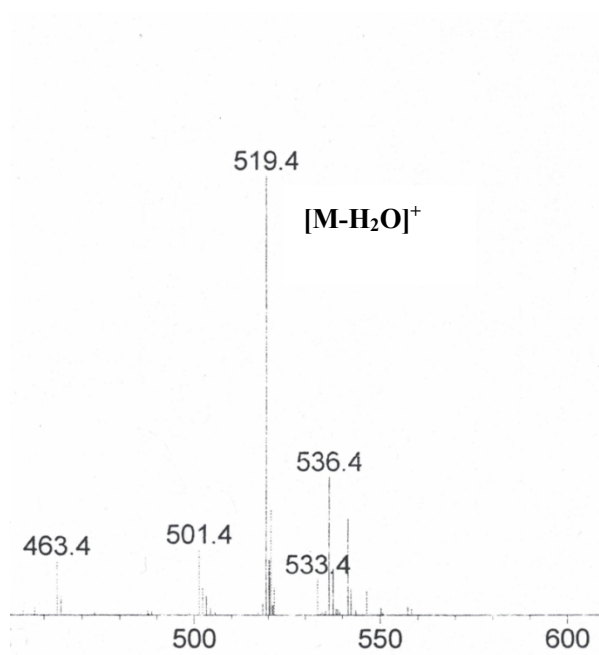
Figure S3. The ^{1}H-NMR spectrum of diMT-Boc.

Figure S4. The ESI-MS spectrum of diMT-Boc.

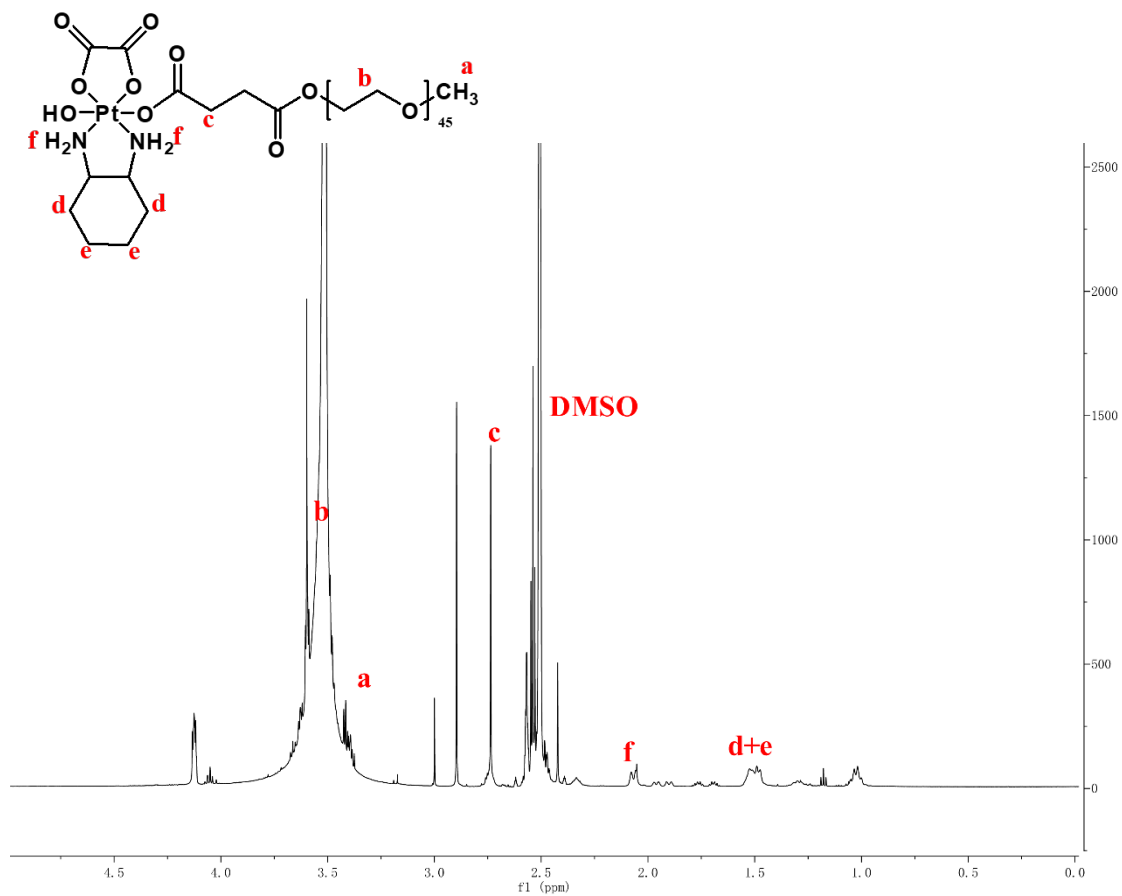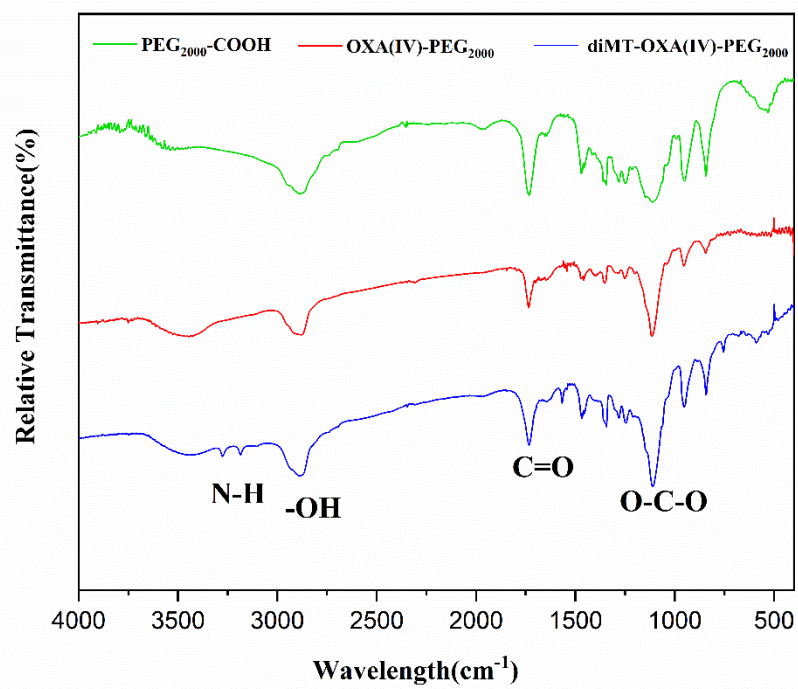Figure S5. The ^{1}H-NMR spectrum of OXA(IV)-PEG2000.

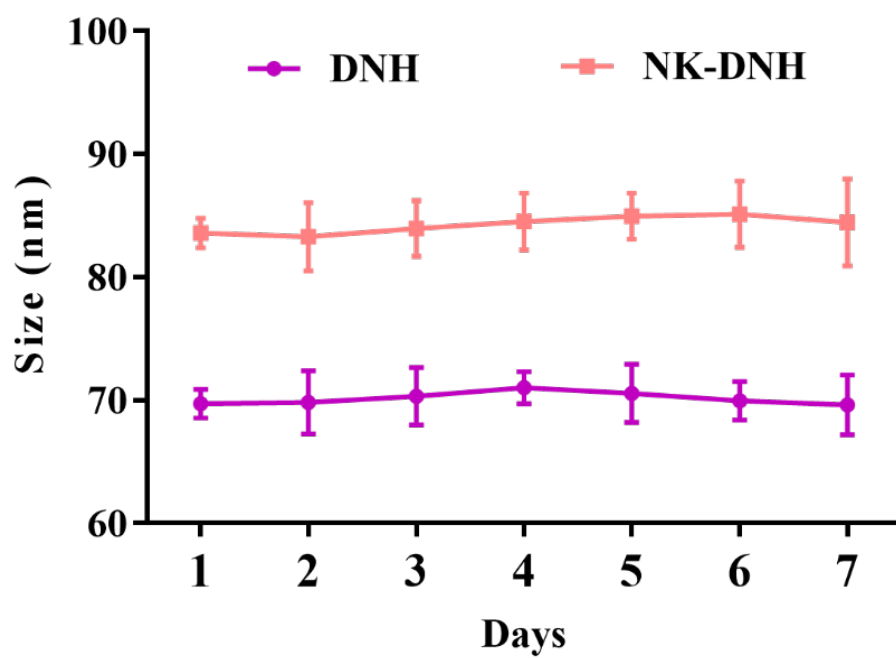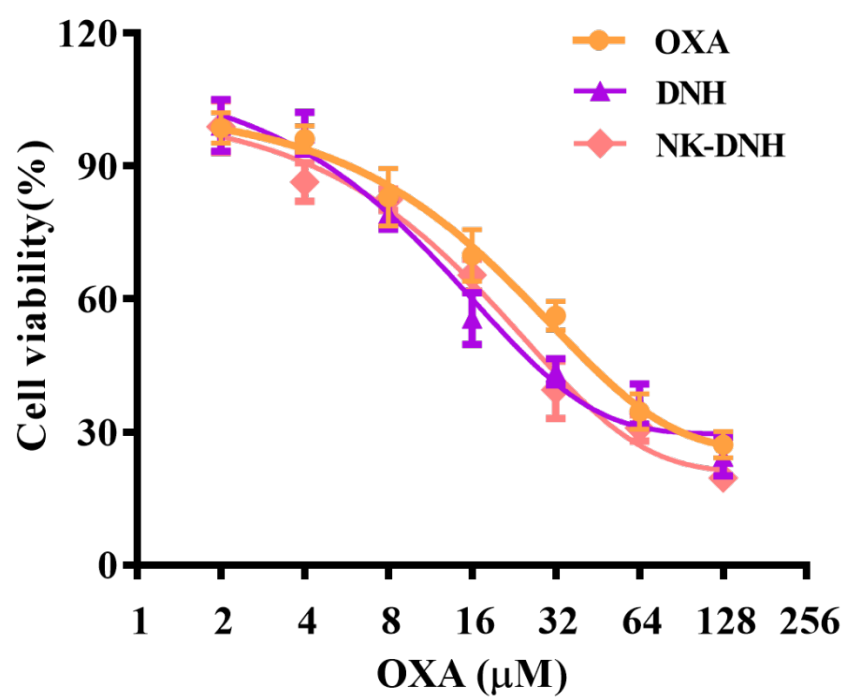Figure S6. The FT-IR spectrum of OXA(IV)-PEG$_{2000}$, PEG$_{2000}$-COOH and diMT-OXA(IV)-PEG$_{2000}$.

Figure S7. Stability of DNH and NK-DNH in PBS.

Figure S8. Cytotoxicity of DNH and NK-DNH against a human breast cancer cell line MCF-7.
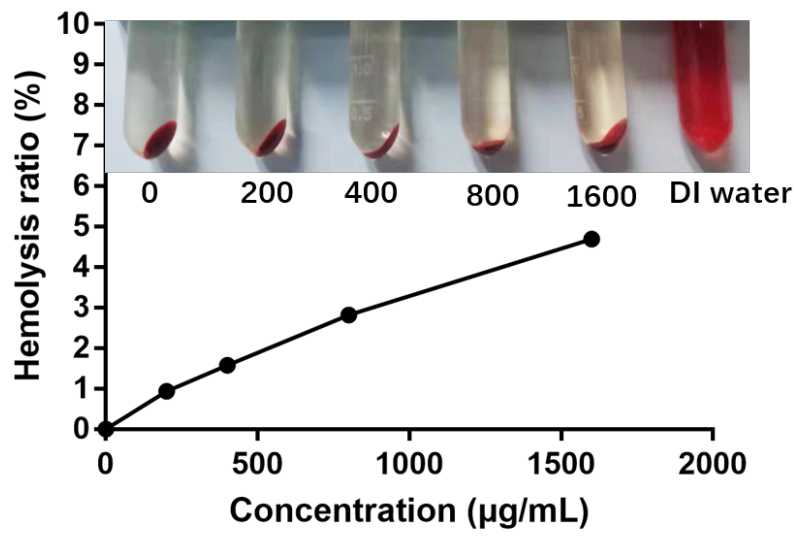
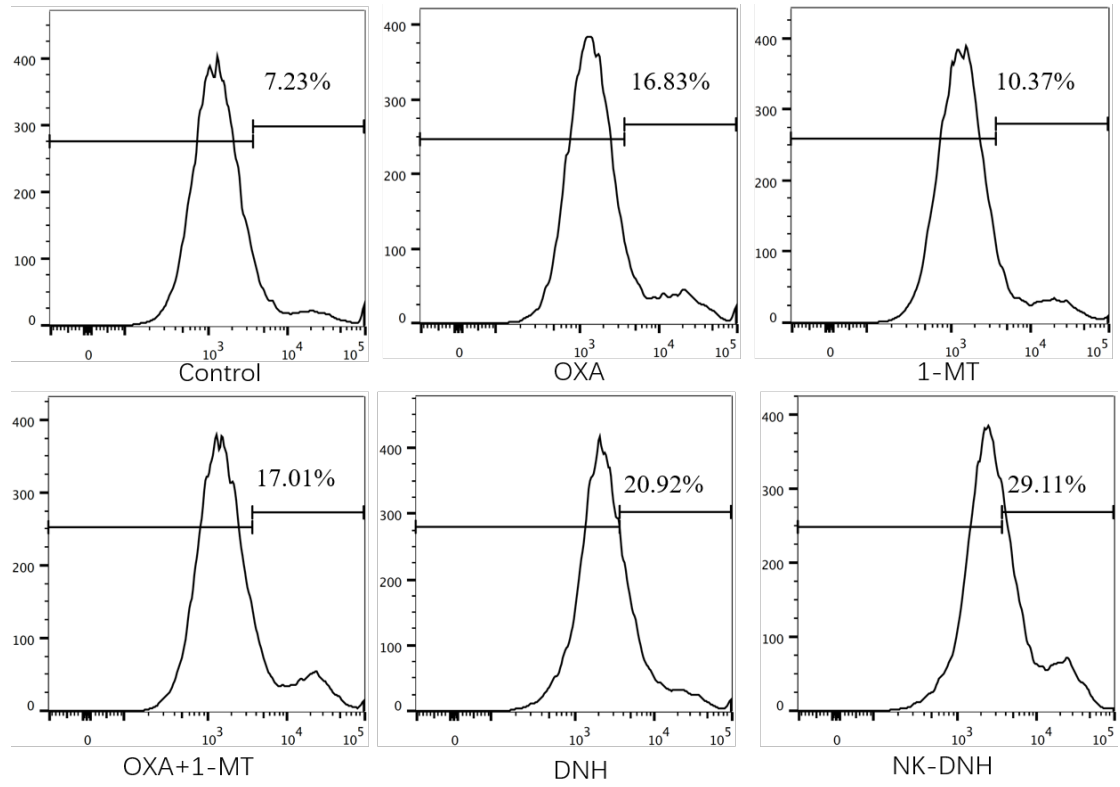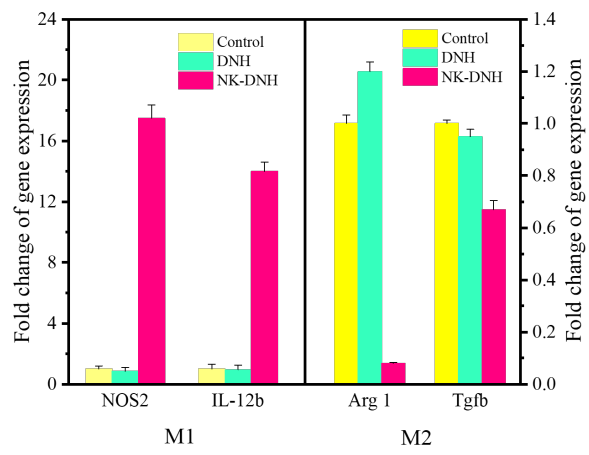Figure S9. Hemolysis ratio of NK-DNH at different concentrations.

Figure S10. The percentages of CD3$^+$ cell in tumors with different treatments.

Figure S11. Gene signs of M1- and M2-macrophage activation in tumor tissues.
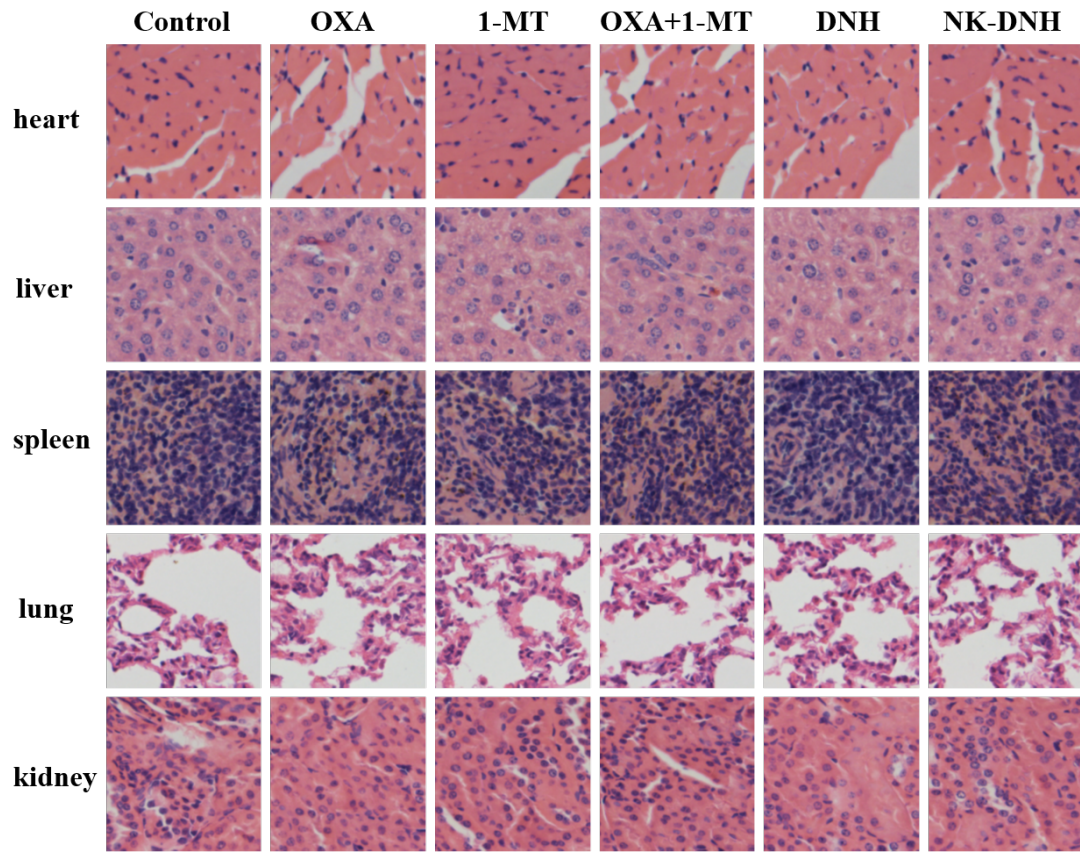
Figure S12. H&E staining assay of different organs after different treatments in 4T1 tumor models.