

Lipid-based Breast Cancer Therapy: Combined Cancer Chemotherapy Based on Doxorubicin-Palmitic Acid-Loaded PLGA Nanoparticles

Introduction

- Doxorubicin (dox) is effective in treating various types of cancer, but it has poor tumor selectivity, tumor cells develop resistance to it and it has serious side effects on healthy tissues and cells.
- Palmitic acid (PA) exhibits anti-inflammatory, metabolic modulating and immunomodulatory effects, as well as antitumor activity in several types of tumors. Its cellular impermeability and precipitation in aqueous solutions limits the use of PA.
- Taking advantage of nanotechnology for drug delivery, we prepared PLGA-nanoparticles loaded with PA and dox and studied their anti-tumor effect in a mouse model of breast cancer.

Objectives

- Development of an immunochemotherapy combination strategy based on targeted delivery of Dox-PA-PLGA.
- PA to make cancer cells more susceptible to the actions of chemotherapeutic drugs.

Methods

1 Preparation of PLGA nanoparticles

Use water-in-oil-in-water (W1/O/W2) double emulsion solvent evaporation technology to make NPs.

2 Characterization of PLGA nanoparticles

The morphology, particle size, zeta potential, PDI, drug loading and the percentage of dox and PA cumulative release from NPs were measured.

3 Evaluation *in vitro*

Cell Viability and invasion assay, cellular uptake, apoptosis assay.

4 Evaluation *in vivo*

Evaluate tumor growth, apoptosis, metastatic niches, and organ-specific toxicity.

Results

Characterization of NPs

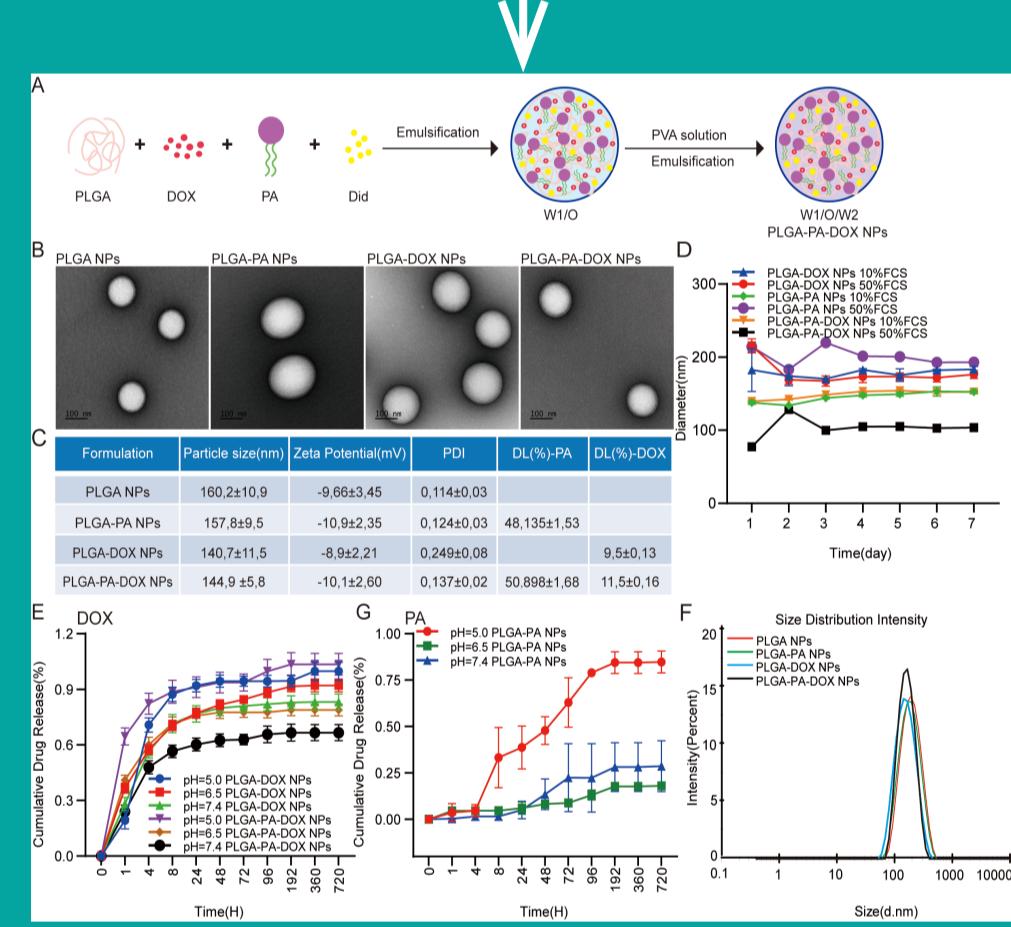


Fig. 1, Physical and chemical properties of NPs.

Cell viability

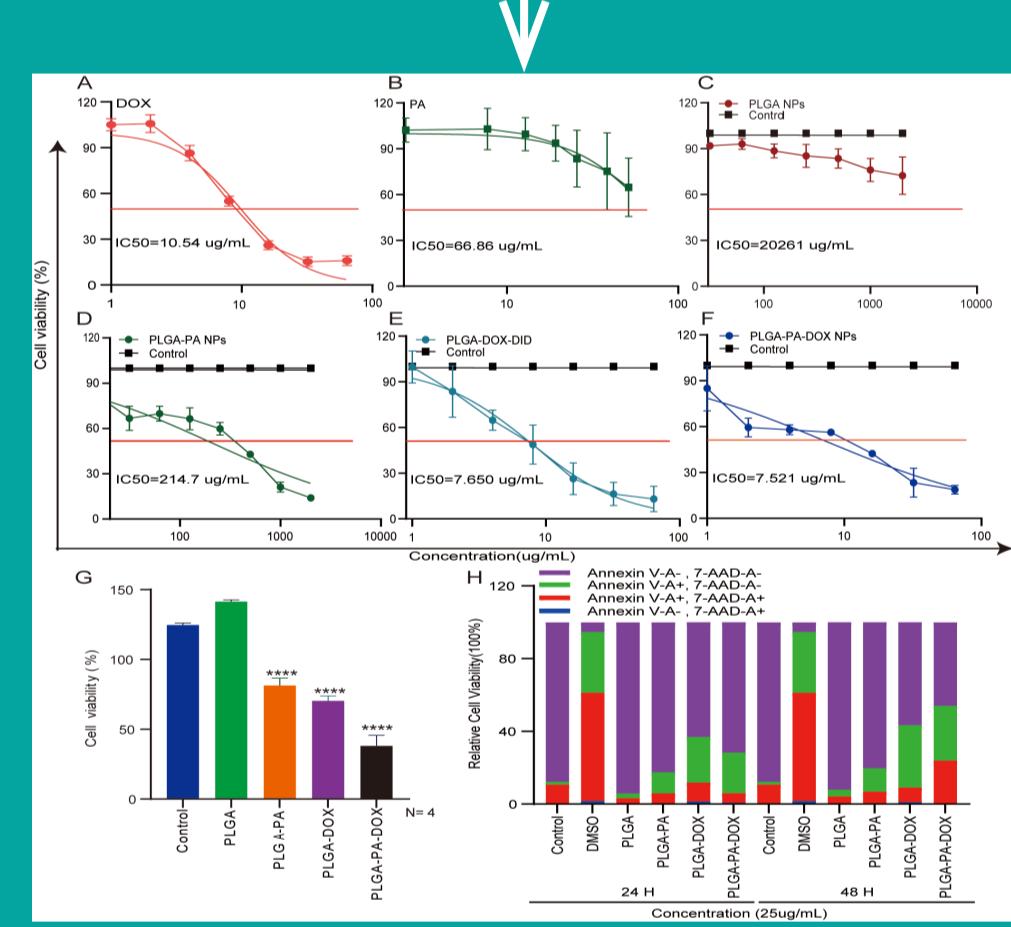


Fig. 2, Effect of DOX, PA or NPs on apoptosis.

Cell uptake of NPs

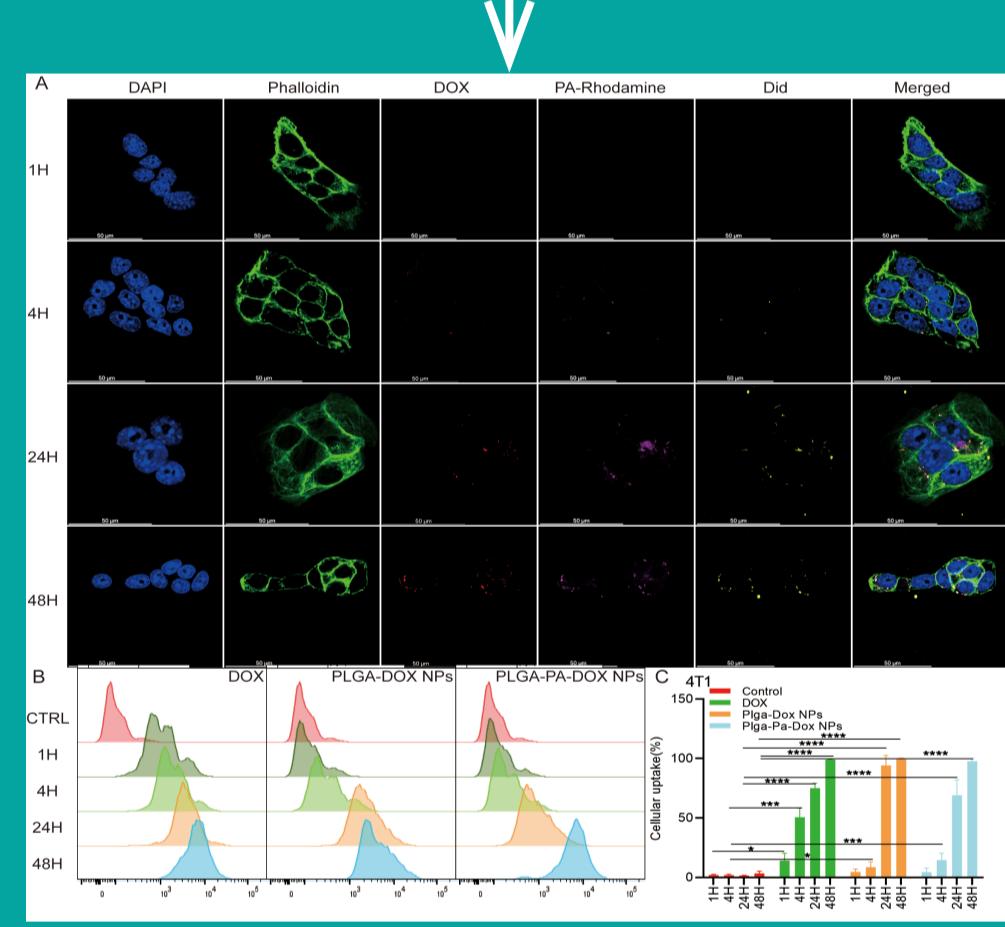


Fig. 3, Cellular uptake of NPs.

Invasion Assay

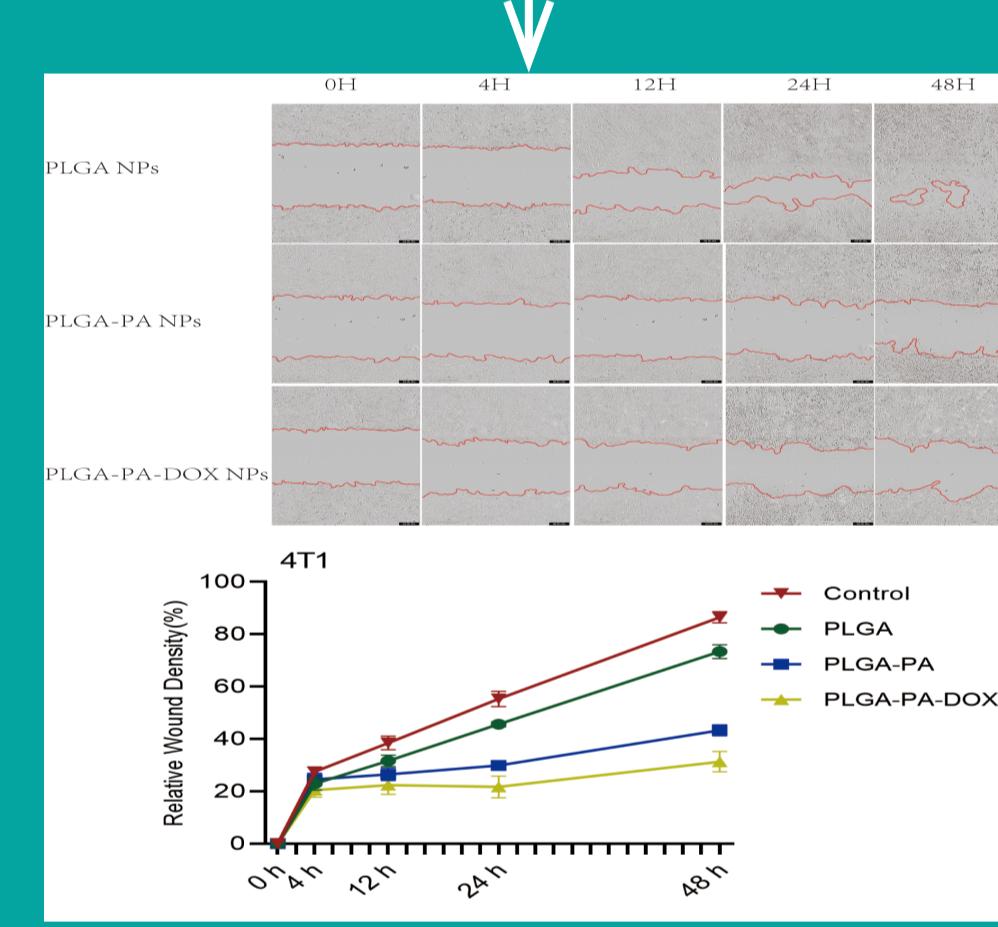


Fig. 4. NPs encapsulating PA inhibit the migration and invasion of 4T1 cells.

Evaluation in vivo

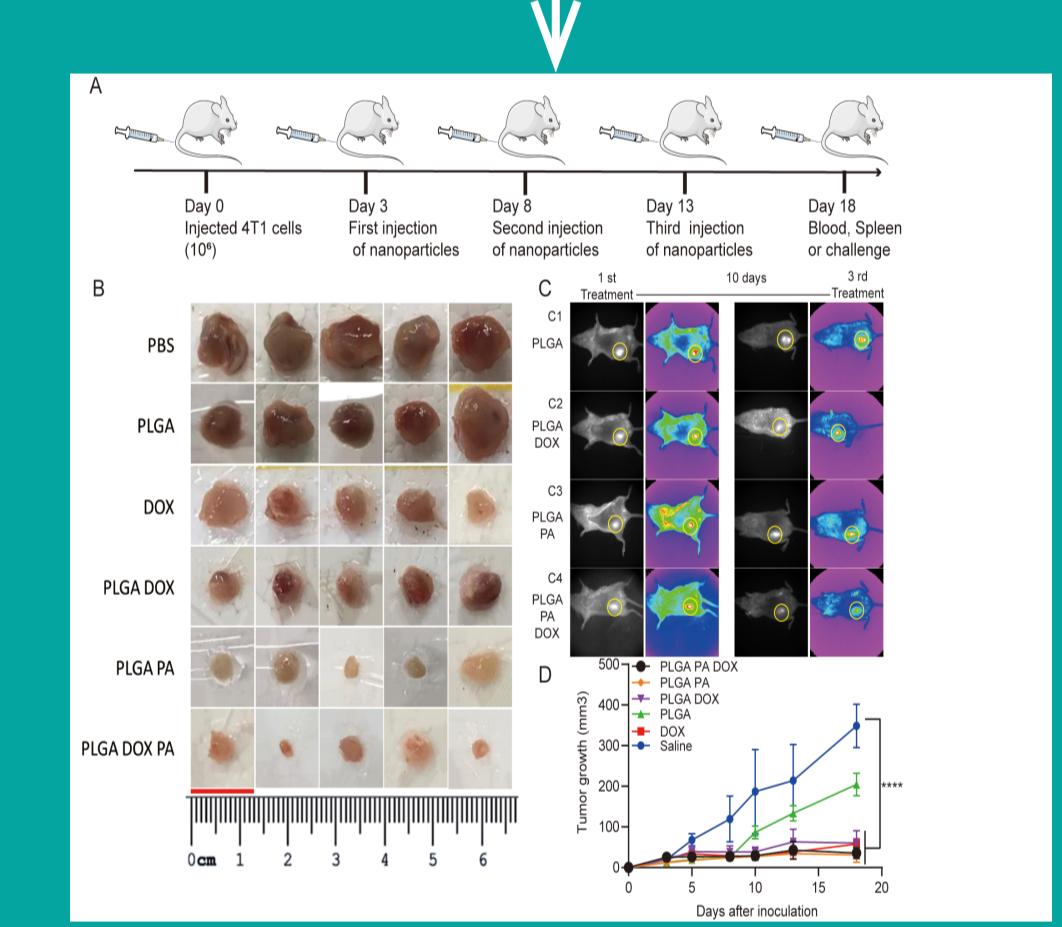


Fig. 5, Inhibition of tumor growth.

The effect in the TME

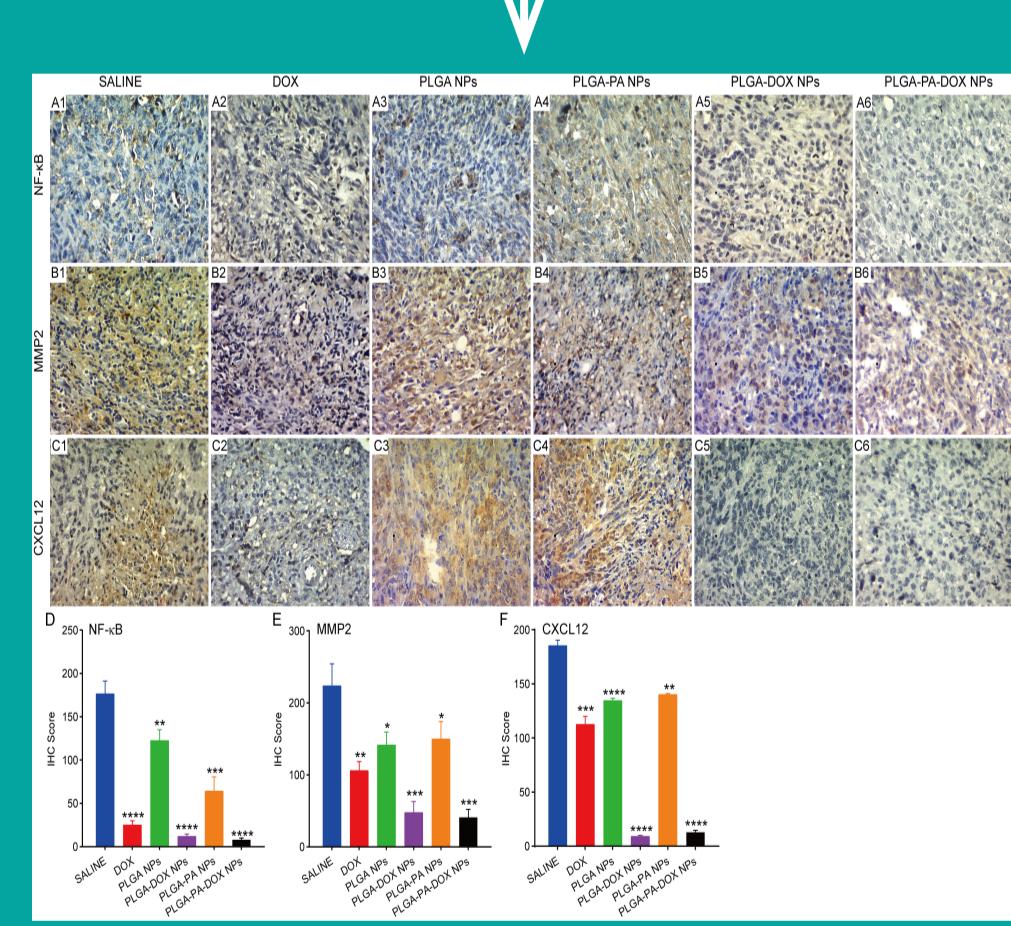


Fig. 6, Evaluation of metastatic niches.

The effect in the TME

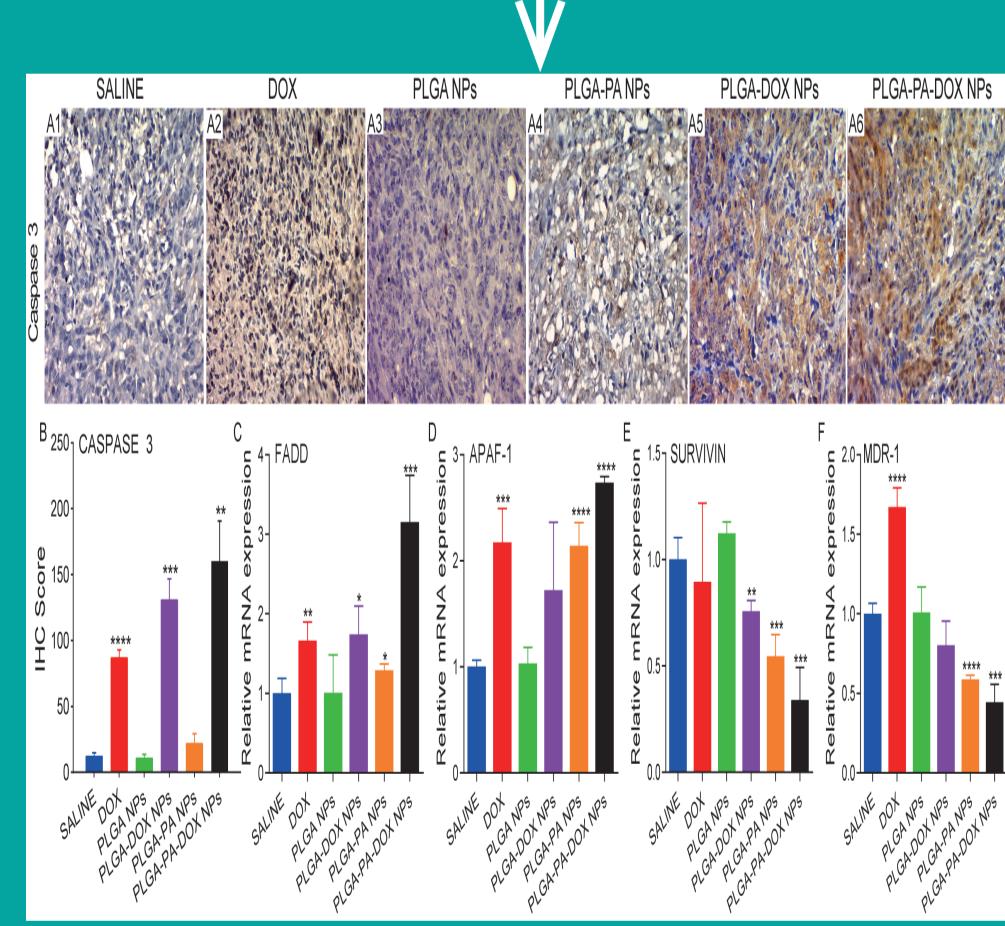


Fig. 7, Assessment of cell death, survival and drug resistance in the tumour microenvironment.

Metastatic niches

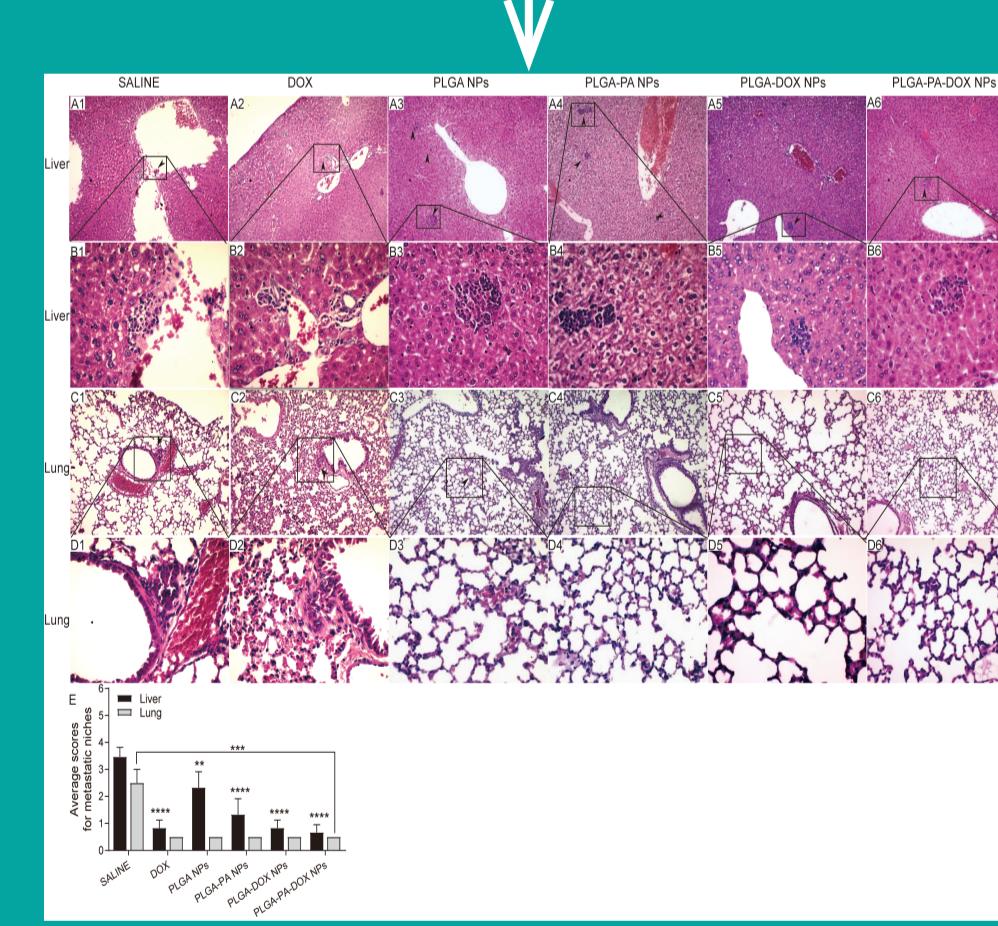


Fig. 8, Assessment of intracellular signaling regulation in the tumor microenvironment.

Conclusions

- PLGA-PA-DOX NPs were successfully formulated and were stable over time.
- The combined use of PA and DOX has a significant effect on cell viability, cancer cell migration and invasion *in vitro*.
- In vivo*, PLGA-PA-DOX NPs not only significantly inhibited breast cancer cell proliferation and reduced drug resistance, but also significantly inhibited tumor metastasis in the lung and liver.

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