



Inhaled Tumor-Responsive MoS₂ Nanoflowers Enhance Locoregional Therapy in Orthotopic Lung Cancer

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INTRODUCTION

BACKGROUND / INTRODUCTION

- Systemic chemotherapy is limited by poor lung-tumor selectivity, off-target toxicity and treatment resistance.
- Aerosol inhalation may increase pulmonary exposure while reducing systemic distribution.

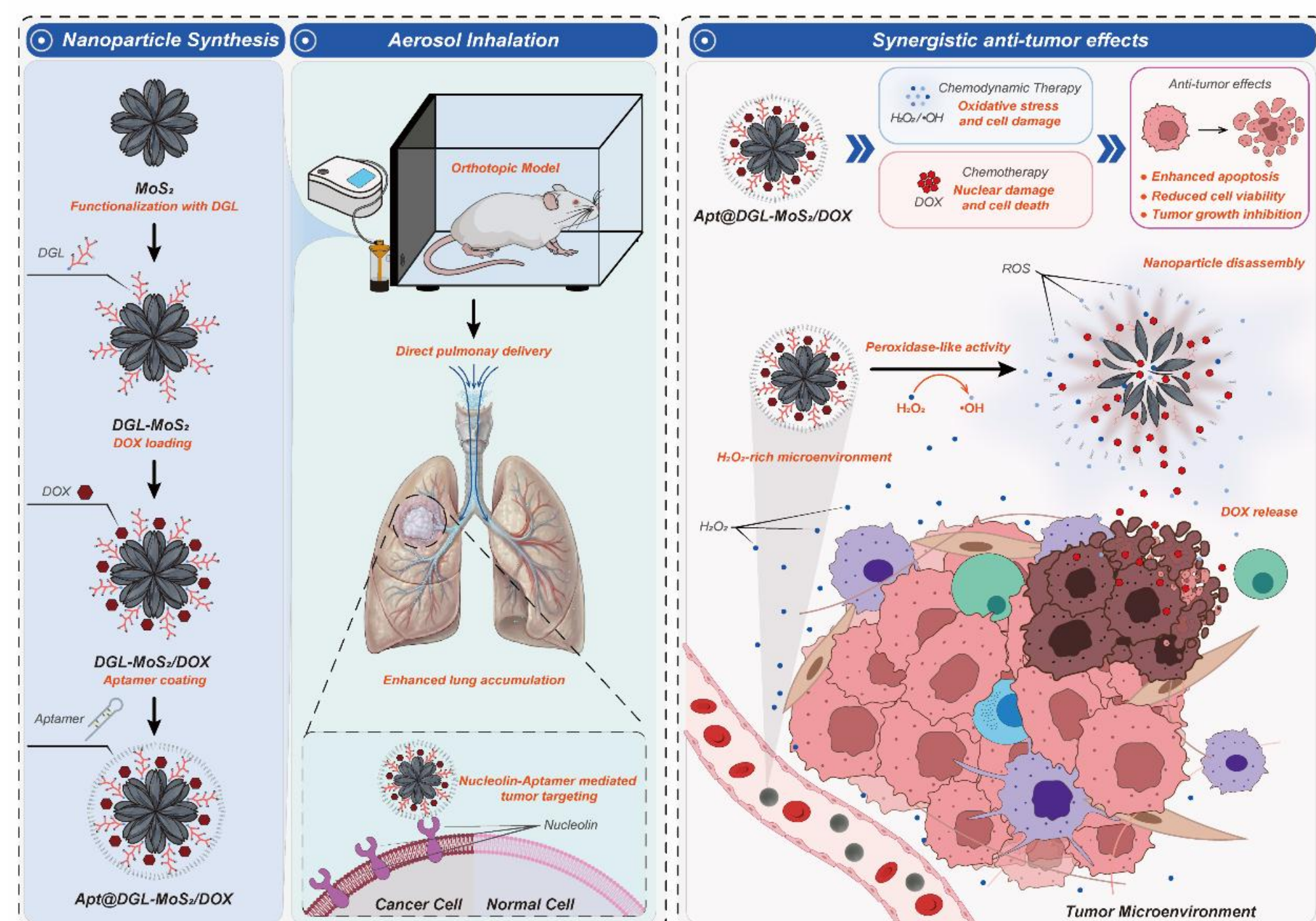
OBJECTIVE

- To develop an inhalable aptamer-gated metallic MoS₂ nanoflower loaded with doxorubicin (Apt@DGL-MoS₂/DOX) that integrates (i) local lung delivery, (ii) AS1411-mediated tumor targeting, (ii) H₂O₂-responsive drug release, and (iv) chemodynamic therapy for orthotopic lung cancer.

METHODS

- Metallic MoS₂ nanoflowers synthesized, coated with DGL, loaded with DOX and decorated with AS1411.
- Characterization: TEM, DLS, zeta potential, stability, ROS generation, and H₂O₂-responsive drug release.
- In vitro: Uptake (confocal/flow), cytotoxicity, apoptosis.
- In vivo: Orthotopic LLC-luciferase lung cancer model. Biodistribution compared aerosol inhalation vs IV.
- Therapy: Aerosol dosing every 3 days for 5 doses.

NANOPARTICLE DESIGN



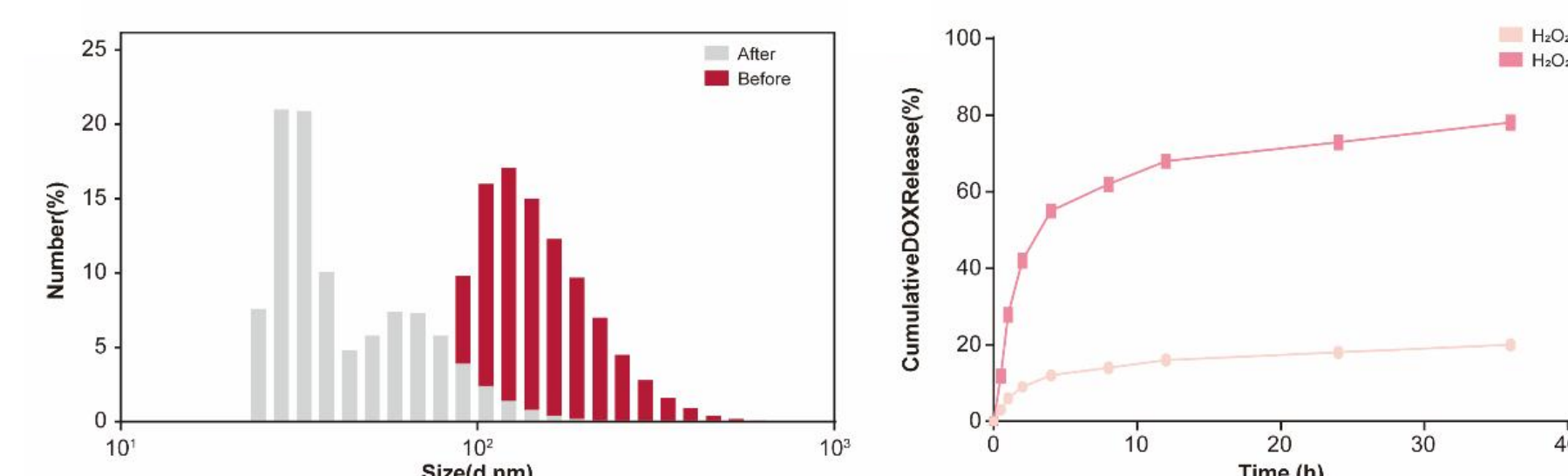
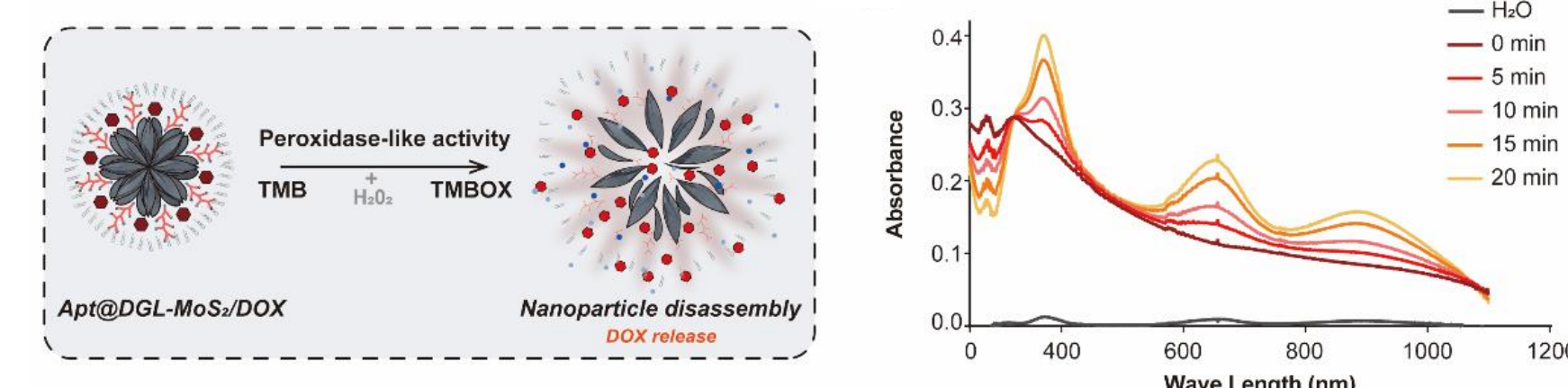
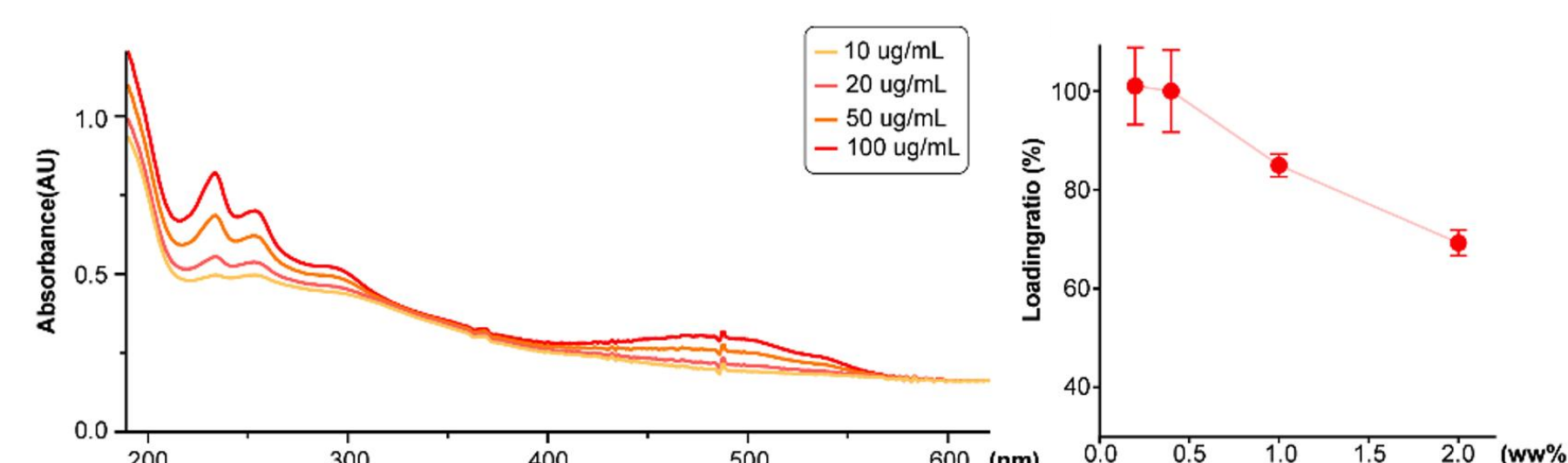
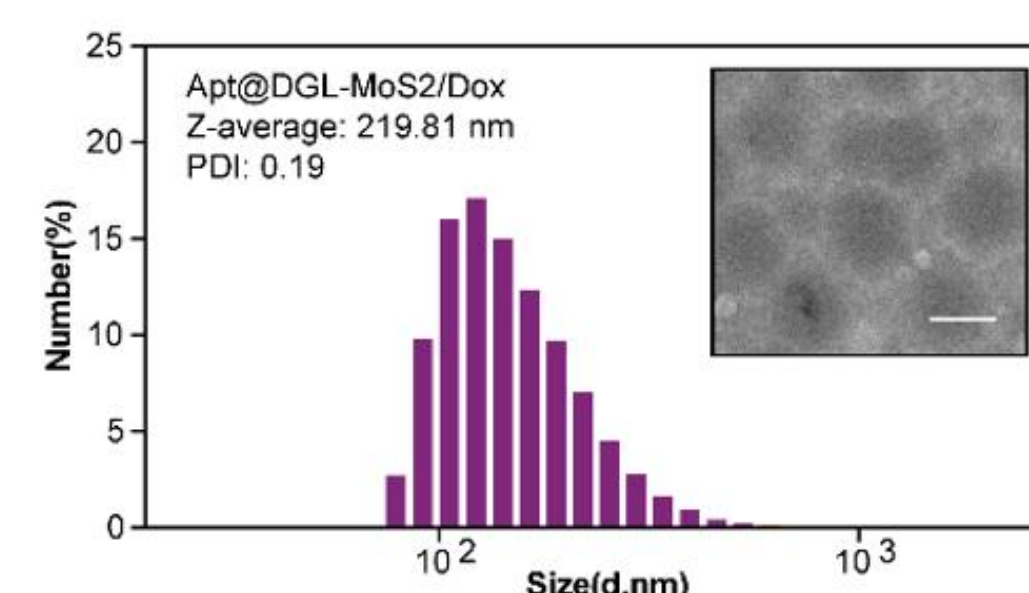
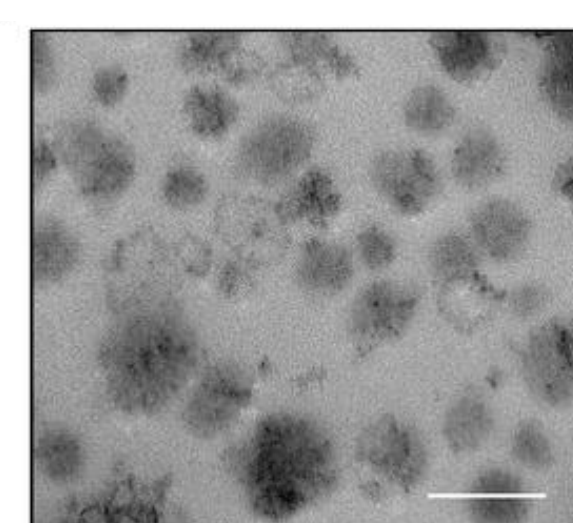
RESULTS - IN VITRO CHARACTERIZATION & ANTITUMOR ACTIVITY

≈ 225 nm
Hydrodynamic Size

> 75 %
DOX Release In
H₂ O₂

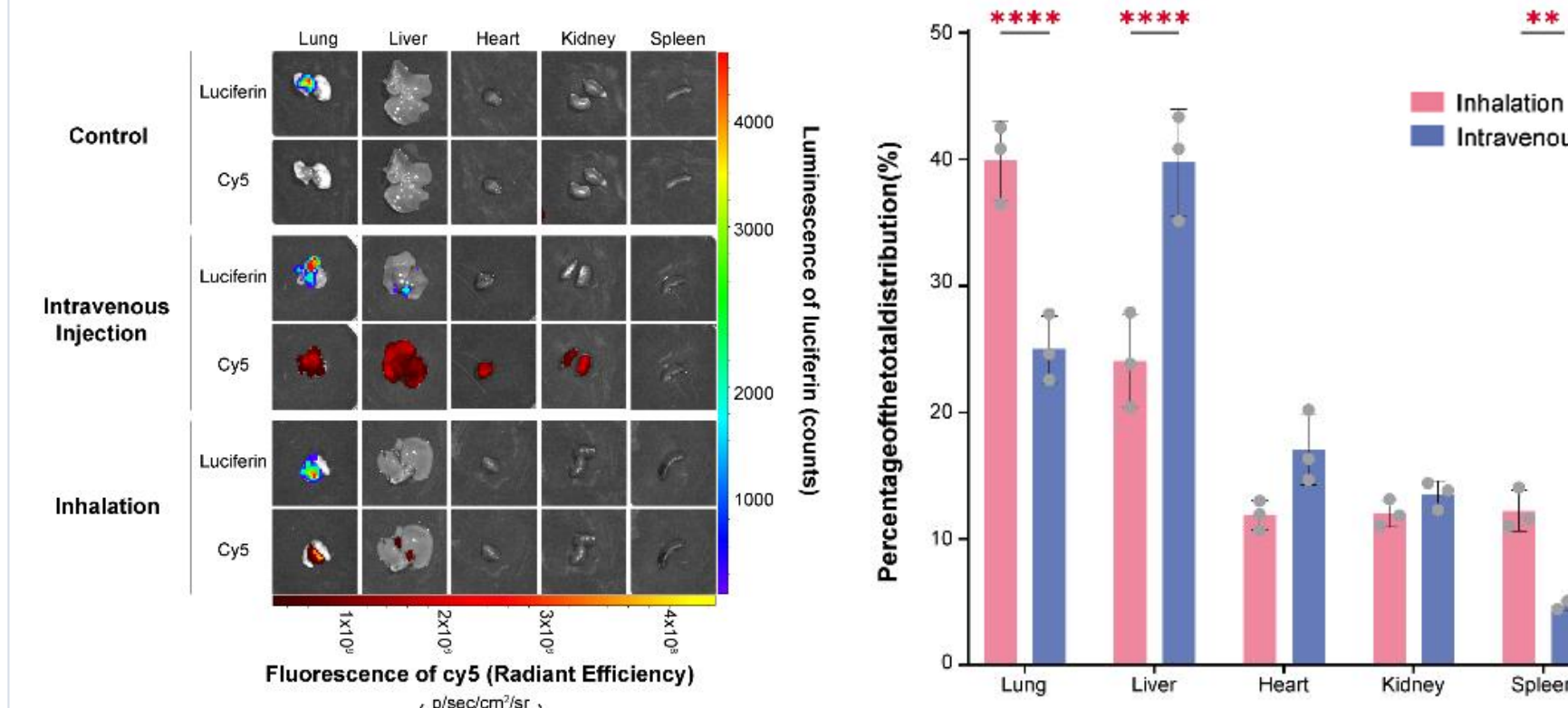
P < 0.01
Pulmonary Accumulation

P < 0.001
Tumor Suppression



RESULTS - IN VITRO EFFIVAVY& BIOSAFETY

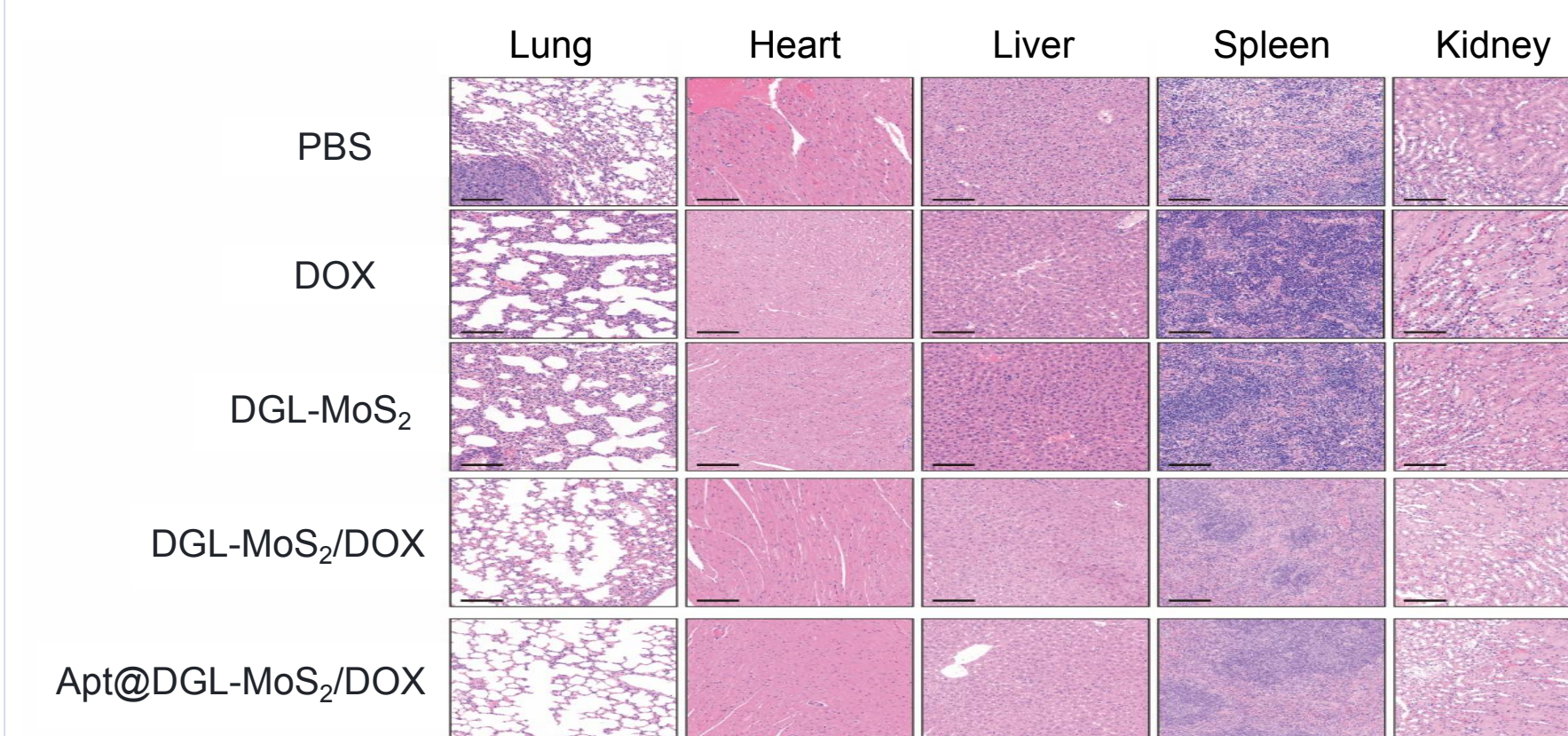
A Biodistribution (Ex vivo fluorescence, 24 h)



B In vivo antitumor efficacy (LLC-luc orthotopic model)



C Biosafety (H&E staining, Day 15)



CONCLUSION

Inhaled Apt@DGL-MoS₂/DOX achieves tumor-responsive drug release and chemodynamic therapy with dominant lung and tumor accumulation, leading to superior antitumor efficacy and minimal off-target toxicity. This platform represents a promising strategy for safe and effective locoregional therapy of lung dominant cancers.

FUTURE DIRECTIONS

- Optimize aerosol performance and device compatibility.
- Define pharmacokinetics, clearance, and long-term safety.
- Evaluate immune modulation and combination therapies.
- Validate efficacy in additional models and metastasis settings.