A Cryogel-Based Dendritic Cell Vaccine Enhances Breast Cancer Post-Surgical Immunotherapy

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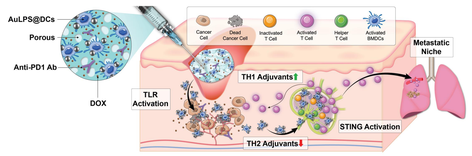
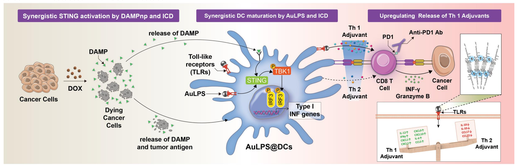
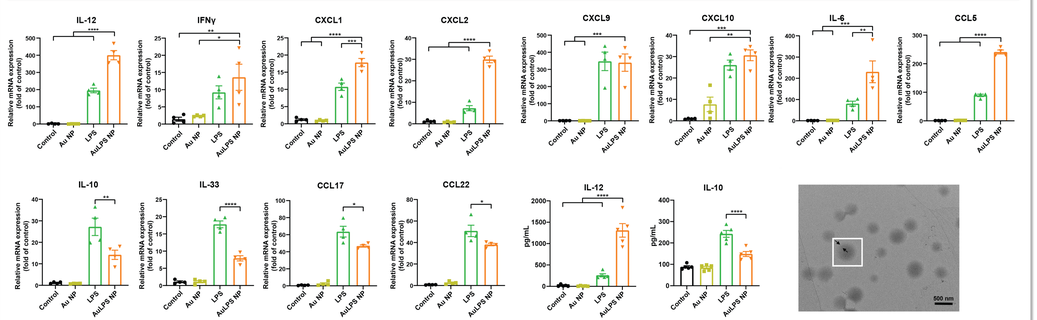
Abstract

Triple negative breast cancer (TNBC) is one of the most aggressive malignancies and caused high risk of cancer related mortality worldwide. Surgical removement of the primary tumor is the primary intervention for TNBC patients. However, the residual cancer recurrence often contributes to a worse cancer progression and tumor metastasis. Recently, the immunotherapy dramatically changes the way in cancer treatment. The combination between surgery, chemotherapy and immunotherapy results in better therapeutic efficiencies against TNBC. Serve as one of the immunotherapeutic, dendritic cell (DC) vaccine plays a critical role for boosting anti-tumor immune activation through evoking the adaptive immune response. However, the therapeutic efficiency is often affected by the immunosuppressive tumor microenvironment that hinder the migration of DCs to lymphoid organ to prime T cells and induce the tolerance of DCs leading to the failure of DC maturation. Therefore, In this study, we developed a DC-based cancer vaccine by encapsulating AuLPS NP loaded DCs, Dox and anti-PD1 antibody in an GelMA cryogel scaffold. The vaccine facilitated the DCs maturation and migration to the lymphoid tissue which generate a potent anti-cancer immunity against the post surgical tumor recurrence and metastasis in mouse TNBC model.

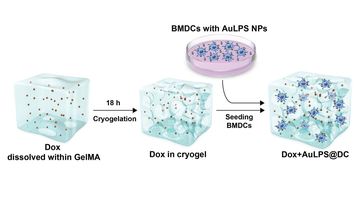


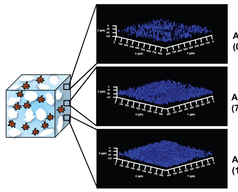


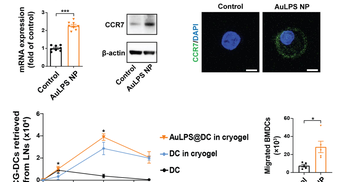
1. AuLPS NP induce Th1 and STING while decreasing Th2 response in BMDCs

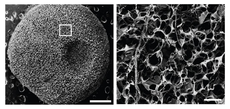


2. Establishment of Dox and AuLPS NP treated BMDCs loaded GelMA cryogel vaccine

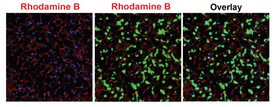








Characterization of Cryogel	
Pore Size (μm)	63.81 ± 11.37
Porosity (%)	89.37 ± 7.96
Interconnectivity of Pores (%)	92.73 ± 0.46
Compressive Modulus (kPa)	1.003 ± 0.150
Dox Encapsulation Efficiency (%)	62.87 ± 6.14
BMDC Seeding Efficiency (%)	80.74 ± 2.60



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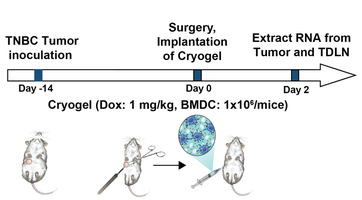
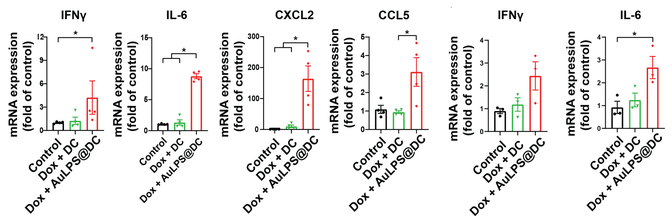
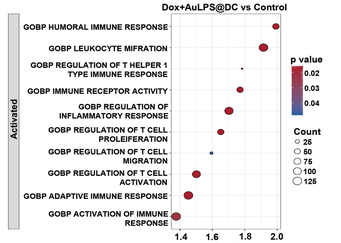
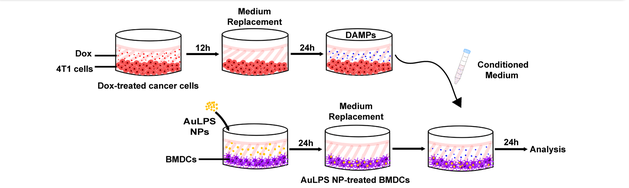
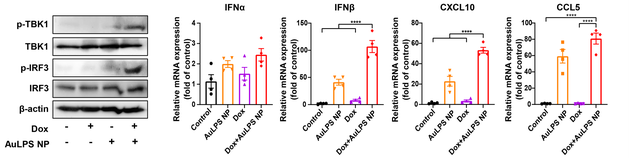


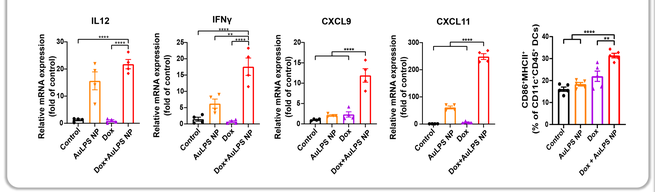




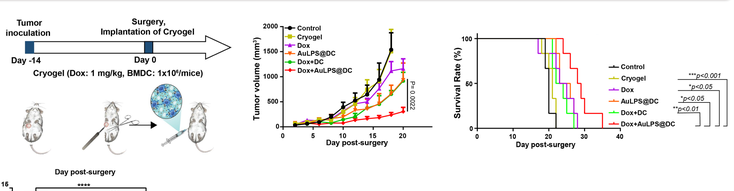
3. Dox synergize with AuLPS NP, induceing STING pathway with enhanced Th1 response and DC activation

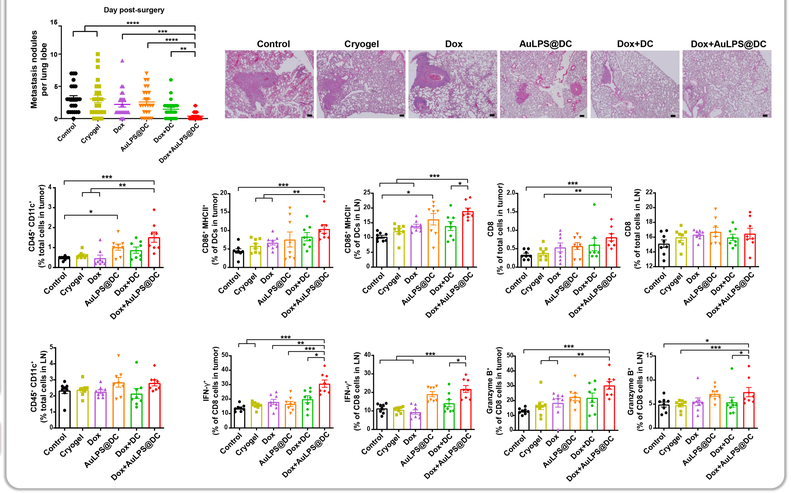






4. Dox and AuLPS NP loaded cryogel vaccine suppress tumor recurrence and metastasis by activating CD8 T cell response





5. Combining with ICI enhanced the therapeutic efficiency against post surgical TNBC