Next-generation nanomaterials against breast cancer

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Nanotechnologies

INTRODUCTION

Breast cancer is the second major cause of **brain metastasis**. Patients with this disease most often have a life expectancy of lower than one year and therefore alternative therapeutic approaches must be considered and used.

Cancer vaccines hold great promise by re-educating T-cell responses to boost regression and inhibit metastasis. However, considering the **complex** and **dysfunctional tumor microenvironment (TME)** cellular network, novel combinatorial regimens are rationally designed to modulate multiple suppressive tumor-immune-stromal cell cross-talks, to render tumor cells highly susceptible for recognition and destruction by T cells. The **myeloid-derived suppressor cells (MDSC)** and regulatory dendritic cells (DC) are examples of **immunosuppressive** cells found at the TME of different tumors. **Ibrutinib** is thus a promising small molecule with an immune-modulatory effect important to improve anti-tumor immune responses against this aggressive disease.

OBJECTIVES

Development of a targeted "dual immunotherapy" combining DC-targeted nanoparticles (NP) with a TME-targeted nanogel to re-educate immune and stromal cell functions within the breast cancer metastases niche. This approach will increase the recruitment of effector immune cells while re-shaping pro-tumorigenic MDSC-mediated immune suppression within tumor site, thus overcoming non-responsiveness of dysfunctional T cells.

- **NP1** is a DC-targeted NP that **mimics cancer cells** full of tumor specific antigens to improve their recognition and capture by DC at the periphery, while re-shaping germinal centers.
- **NP2** is a TME-targeted NP based on pH-responsive methacrylic acid (MAA) hydrogels that will improve the accumulation of ibrutinib within the TME.

RESULTS – NP1

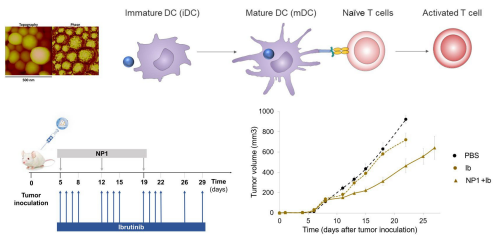

Fig. 1. Timeline, treatment schemes and tumor growth curve.

RESULTS – NP2

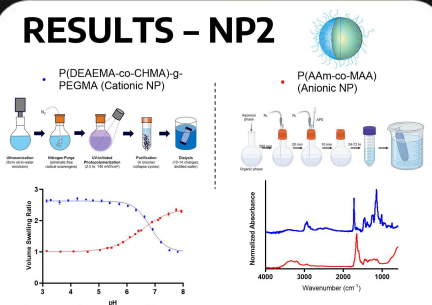

Fig. 2. Volume swelling curves.

Blue line – cationic NP
Red line – anioninc NP

Fig. 3. Fourier-Transform Infrared Spectroscopy.

FUTURE WORK

The combination of ibrutinib with NP1 controlled the tumor growth in 4T1-bearing mice, supporting its potential application to locally regulate TME immune suppression following its delivery by NP2. Ongoing studies aim to characterize the anti-tumoral effect of NP2 isolated and combined with NP1.

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