Nano Biomed Eng
2018, Special Issue: 310.

Conference Proceeding

Combining Nanovaccine and Radiotherapy to Revert the Immunosuppressive Environment in Tumor

Min Luo[1,2], Zhida Liu[3], Yangxin Fu[3], Jinming Gao[2]

[1]Children's Hospital and Institutes of Biomedical Sciences, Fudan University, Shanghai 200032, China.
[2]Department of Pharmacology, Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, Texas 75390, USA.
[3]Department of Pathology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, Texas 75390, USA.

Corresponding authors. E-mail: jinming.gao@utsouthwestern.edu; luo_min@fudan.edu.cn

Presented: 2018 Chinese Conference on Oncology. Shenyang, China, Aug. 17-19, 2018; **Published:** Oct. 17, 2018.

Citation: Min Luo, Zhida Liu, Yangxin Fu, and Jinming Gao, Combining Nanovaccine and Radiotherapy to Revert the Immunosuppressive Environment in Tumor. *Nano Biomed. Eng.*, 2018, Special Issue: 310

Abstract

Generation of tumor-specific T cells is critically important for cancer immunotherapy. However, T cells alone are not adequate to eliminate well-established tumors due to the immune suppressive environment. We had previously reported a STING-activating nanovaccine by a simple physical mixture of an antigen with a polymeric nanoparticle, PC7A NP, which generated robust T cell response with low systemic cytokine expression. Increasing evidences showed that RT (radiation therapy) can augment adaptive T cell responses to tumors, thereby decreasing immunosuppression to mediate tumor eradication. But based on clinical evidence, RT alone is unlikely to induce or sustain an immune response that is therapeutically useful. Here we hypothesize that combination of PC7A nanovaccine with local RT will revert the immunosuppressive environment in tumors and overcome tumor resistance to RT or nanovaccine alone. To test the therapeutic effect of nanovaccine in addition to local RT-mediated tumor regression, we utilized an established HPV related TC-1 (expressing the E6-E7 HPV gene) tumor model. Vax alone and RT alone were used as controls to assess the synergy effects. Data show that when mice were treated with Vax at 5 days after tumor cell inoculation, 60% mice were cured and with tumor free for 60 days. However, when mice were treated with Vax 10 days after tumor cell inoculation (tumor size 100-200 mm^3), tumors showed initial shrinkage a week after one administration. The Vax generated T cells were not sufficient to reject the tumors, and all tumors relapsed a month later. When Vax was combined with radiation in the TC-1 model, it led to a dramatic synergistic effect with long term regression of large established HPV tumors. Percentage of tumor specific CD8+ T cells greatly increased in tumors after combination therapy compared to either single treatment alone. Further mechanistic studies are still ongoing.

Keywords: PC7A nanovaccine; T cells; Cancer immunotherapy; Radiotherapy