

Targeted Photodynamic Therapy for Intraperitoneal Ovarian Cancer, A Way to Stimulate Anti-Tumoral Immune Response

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Abstract : Ovarian cancer (OC) is one of the most defying diseases in gynecologic oncology. Even though surgery remains crucial in the therapy of patients with primary ovarian cancer, recurrent recidivism calls for the development of new therapy protocols to propose for patients dealing with this cancer. FR α is described as a tumor-associated antigen in OC, where FR α expression is usually linked with more poorly differentiated, aggressive tumors. The Photodynamic treatment (PDT) available data have shown improvements in the uptake of small tumors and in the induction of a proper anti-tumoral immune response. In order to target specifically peritoneal metastasis, which overexpress FR α , a new-patented PS coupled with folic acid has been developed in our team. Herein we propose PDT using this new patented PS for PDT applied in an in vivo mice model. The efficacy of the treatment was evaluated in mice without and with PBMC reconstitution. Mice were divided into four groups: Non-Treated, PS, Light Only, and PDT Treated and subjected to illumination by laser set at 668nm with a duration of illumination of 45 minutes (or 1 min of illumination followed by 2 minutes of pause repeated 45 times). When mice were not reconstituted and after fractionized PDT protocol, a significant decrease in the tumor volume was noticed. An induction in the anti-tumoral cytokine IFN γ chaperoned this decrease while a subsequent inhibition in the cytokine TGF β . Even more crucial, when mice were reconstituted and upon PDT, the fold of tumor decrease was even higher. An immune response was activated decoded with an increase in NK, CD3 +, LT helper and Cytotoxic T cells. Thereafter, an increase in the expression of the cytokines IFN γ and TNF α were noticed while an inhibition in TGF β , IL8 and IL10 accompanied this immune response activation. Therefore, our work has shown for the first time that a fractionized PDT protocol using a folate-targeted PDT is effective for treatment of ovarian cancer. The interest in using PDT in this case, goes beyond the local induction of tumor apoptosis only, but can promote subsequent anti-tumor response. Most of the therapies currently used to treat ovarian cancer, have an uncooperative outcomes on the host immune response. The readiness of a tumor adjuvant treatment like PDT adequate in eliminating the tumor and in concert stimulating anti-tumor immunity would be weighty.

Keywords : folate receptor, ovarian cancer, photodynamic therapy, humanized mice model

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