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Tumor destruction in situ as a tool to trigger a robust anti-tumor immune response

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Abstract

The role of the immune response in tumor development and treatment is a complicated issue. Many elements are involved such as the variety of tumor types, the organism genetics, the complexity of the immune response, metabolism, age, and the microbiome to name a few.
The goal of cancer immunotherapy is to induce tumour regression, eradicate minimal residual disease, establish lasting antitumour memory and avoid non-specific or adverse reactions. Yet, even though about 70 years elapsed since the discovery of tumor antigens, the success of therapeutic cancer vaccines has been very limited and variable. It mainly resulted from the heterogeneity of the tumor and its microenvironment, the presence of immunosuppressive cells and molecules, and tumor escape mechanisms. The failure to develop effective specific tumor vaccines reverted the attention to an observation, which is now 70 years old, “the abscopal effect”. This effect states that irradiation of a tumor site can cause the decrease in size of distant tumor foci [1], an effect which was eventually attributed to the activation of anti tumor immunity.
There is a growing volume of data from both clinical and non-clinical studies that various modalities of *in situ* tumor destruction (ablation) can be a source of tumor antigens that otherwise would be difficult to expose to boost anti-tumor immune responses. The ensued immune reactivity can be further strengthened by both immune and non-immune modulators (2).
Tumor ablation is defined as the direct application of chemical, thermal, radiation or electrical energy to a specific focal tumor to achieve eradication or cytoreduction inducing cellular necrosis. To this effect we developed a novel alpha radiation-based tumor treatment termed “Diffusing alpha emitters Radiation Therapy-DaRT”, which can cause fast tumor cell destruction within several days and trigger specific anti-tumor immunity [3].
The advantages of tumor destruction *in situ*, which facilitate triggering anti-tumor immunity include:
1. Tissue damage which attracts inflammatory cells and causes the release of inflammatory cytokines.
2. The extensive cell death release large quantities of tumor-associated antigens in the context of danger-associated molecular patterns (DAMPs) to the immune system.
3. Elimination of the requirement to identify tumor-specific antigens for each patient.
There are several types of measures which can be taken to promote anti-tumor immunity following *in situ* tumor ablation: i) immune potentiation agents, and ii) agents to counteract suppressive mechanisms.
These findings prompt new ablation modalities and immunological manipulations which will increase the arsenal of the medical staff and promote cancer treatment.
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