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Vaccination with dendritic cells pulsed with glioma killed by photodynamic therapy induces efficient antitumor immunity

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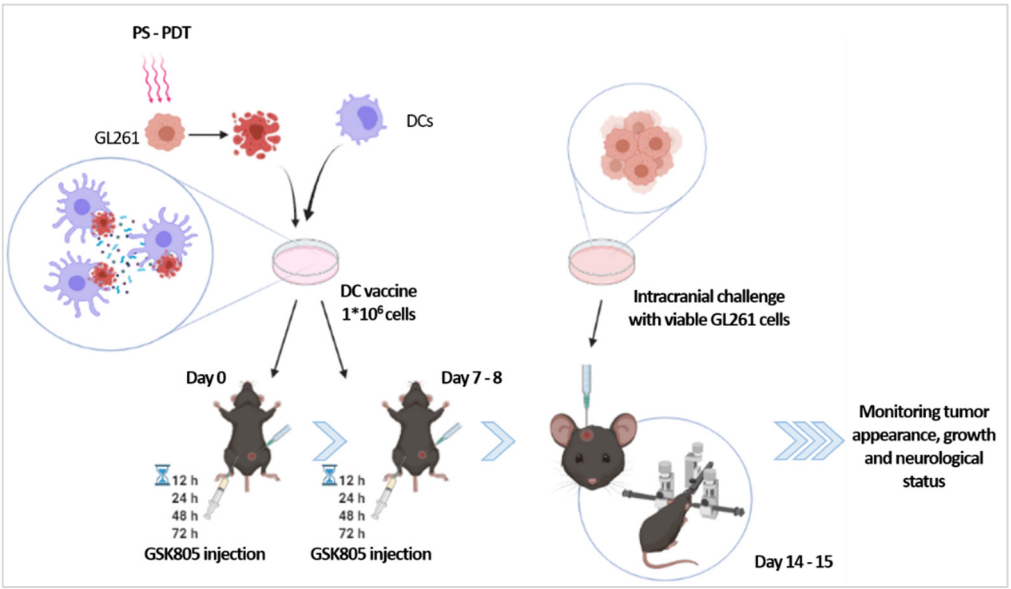
Currently, there are no optimal methods for treated oncological diseases that would ensure the complete recovery of the patient and guarantee the absence of relapse. The immunogenic cell death (ICD) model involves the activation of an antitumor immune response in response to the emission of damage-associated molecules (DAMPs) due to cell death [1]. Photodynamic therapy (PDT) is one of the cancer therapies that can cause ICD.

We have chosen a photosensitizer used in clinical protocols – Photosens (Niopic, Russia). The effectiveness of photosens (PS) has already been shown *in vitro* on the MCA205 line, and a vaccine based on cells induced by photosens-PDT protected mice from tumor development in a syngeneic model [2]. First, we found that, at doses of 20 J/cm^2, they effectively induce regulated cell death in a mouse glioma cell line (GL261). The intracellular distribution of PS was studied using a laser scanning microscope. Tumor cells undergoing PS-PDT-induced cell death emit calreticulin, HMGB1, and ATP, and these are efficiently taken up by bone marrow dendritic cells, which then mature, become activated, and produce IL-6.

Using dying cancer cells induced by photosens-PDT, we demonstrate the efficient vaccination potential of ICD *in vivo.* In the model, activated dendritic cells have become a powerful stimulus for the activation of T-cell populations.

We assessed the survival rate of animals, analyzed the neurological status of the animals during the experiment, visualized the tumor in the brain by magnetic resonance imaging, assessed the size of developing tumors.

The ICD-based DC vaccine demonstrated high efficacy in subcutaneous and orthotopic mice models. By using RNA sequencing to characterize the transcriptional program of ICD based DC vaccine, we identify a high expression of 1357 genes and by assessing their functional relevance in immune responses we observed a robust induction of Tgfb-3, IL-6, IL-23a implicating Th17 immunity. We found that the increased intratumor prevalence of Th17 cells linked genetic signatures is associated with good patient prognosis on The Cancer Genome Atlas low grade glioma cohort. The efficacy of ICD based DC vaccines was significantly reduced by antagonist of RORγt inhibiting the development of Th17 response.



Thus, this indicates the immunogenicity of the death of tumor cells after photodynamic exposure and is the basis for a therapeutic protocol for the using of a dendritic vaccine.
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