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Combination of Phosphatidyl Serine Blockade and STING Stimulation for Cancer Immunotherapy

A novel pharmaceutical combination enhances cancer treatment efficacy by blocking immunosuppressive Phosphatidylserine (PS) signals and boosting anti-tumor immune response.

Immunotherapy is one of the most critical tools available for cancer treatment. However, tumor resistance to immunotherapy can develop over time due to the emergence of an immunosuppressive tumor microenvironment (TME). Phosphatidylserine (PS), a key cellular phospholipid, plays a role in this immunosuppression. Normally, PS present on apoptotic cell membranes attracts phagocytes for removal of the apoptotic cells and simultaneously triggers anti-inflammatory signals for homeostasis. Tumor cells hijack this pathway to avoid the surveillance of the immune system. Research has shown that an increase in PS occurs following radiation or chemotherapy treatment in patients. Counteracting this increase in PS is crucial for effective immunotherapy and reducing TME suppression.

Purdue Researchers have developed a pharmaceutical combination that is able to the block PS and boost the anti-tumor response within cells, allowing for enhanced immunochemotherapy of tumors. The pharmaceutical combination consists of a PS blocker, an immune stimulant, and a chemotherapeutic agent. The PS blocker can be composed of dipicolylamine (DPA) or its metal complex, a metal salt, Annexin V, or an anti-PS antibody. The PS blocker is coupled with an immune stimulant such as a STING agonist or granulocyte-macrophage colony-stimulating factor or any combination of the two. The anti-tumor efficacy of the developed formulation was tested in C57BL/6 mice bearing melanoma and successfully delayed tumor growth with an increase in immune stimulation. The PS blockade therapy can be used to enhance immunotherapy and other standard cancer therapies by circumventing immunosuppressive feedback to the treatment.

Technology Validation:

Technology ID
2023-YEO-70023

Category
Pharmaceuticals/Drug Discovery & Development
Pharmaceuticals/Small Molecule Therapeutics
Pharmaceuticals/Drug Delivery & Formulations

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-Transmission electron microscopy images were taken to identify the coordination of cyclic dinucleotide (CDN) and Zn nanoparticles

-Isothermal titration calorimetry (ITC) was performed to calculate the binding affinity of DPA-Zn to PS

-ITC of CDN-Zn was used to calculate the stoichiometry and dissociation constant

-C57BL/6 mice were inoculated with melanoma for treatment with CDN DPA-Zn formulation

-In vitro release of DPA-Zn or CDN from hydrogels was performed

Advantages:

-Decrease in immune suppression by blockade of PS

-Increase in efficacy of standard cancer therapy drugs

Applications:

-Cancer treatment

TRL: 3

Intellectual Property:

Provisional-Gov. Funding, 2023-10-10, United States | PCT-Gov. Funding, 2024-09-04, WO

Keywords: Immunotherapy, tumor resistance, tumor microenvironment, phosphatidylserine, PS blocker, immune stimulant, chemotherapeutic agent, anti-tumor response, cancer therapy, dipicolylamine