Methods To Enhance Cancer Immunotherapy

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BACKGROUND

Immune checkpoint inhibitors, such as antibodies that block negative regulators of T-cell activation (such as CTLA4 and PD-1/PD-L1), have transformed cancer treatment. However, even in metastatic melanoma and non-small cell lung cancer (NSCLC), malignancies that are highly responsive to immune checkpoint inhibitors (ICI), response rates rarely exceed 40%. Not only that, many common malignances, such as prostate cancer and pancreatic ductal adenocarcinoma, are ICI refractory but causes of treatment failure are largely unknown. It is known though that oxaliplatin triggers a form of cell death that is thought to be immunogenic, whereas the chemical analogue cisplatin does not trigger the same form of immunogenic cell death.

Recent clinical trials have shown that immune checkpoint inhibitors responsiveness is significantly augmented by combining PD-1 signaling inhibitors with platinoid chemotherapeutics. Such results have led to approval of immune checkpoint inhibitors + platinoid combination therapy in NSCLC but the basis for this synergism has not been determined.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed a method for enhancing the therapeutic response to immune checkpoint inhibitors and TCR mediated immunotherapy. Killing of cancer cells by tumor-specific effector CD8+ T cells requires expression of MHC-I molecules on the cancer cell and presentation of relevant tumor antigens by these MHC-I molecules. The invention increases expression of MHC-I molecules on the cancer cell surface and stimulates the induction of MHC-I expression. Antigen presentation is of particular importance in cancers that: a) have low MHC-I expression to start with; b) have down-regulated MHC-I expression as they became refractory to immunotherapy. Importantly, this invention is based on stimulation of a post-translation modification as a pre-requisite for increased MHC-I expression and antigen presentation.

APPLICATIONS

Oxaliplatin treatment also results in induction of a specific receptor, through NF-κB signaling, which potentiates the response of MHC-I-expressing cancer cells to CD8+ T cells that have been reinvigorated by immune checkpoint inhibitors administration. It also offers a method to identify a cancer cell that is amenable to treatment with immune checkpoint inhibitors.

ADVANTAGES

This invention is broadly applicable for the treatment of a number of cancers and offers a novel mechanism for upregulation of MHC molecules.

STATE OF DEVELOPMENT

Experimental stage (in vitro and in vivo data in mouse disease models)

INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

cancer immunotherapy, checkpoint inhibitors, platin-based drugs, MHC-I, antigen presentation, immune checkpoint inhibitors

CATEGORIZED AS

- Medical
  - Disease: Cancer
  - Therapeutics

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