Contact:
Harl Tolbert,
techtransfer@roswellpark.org,
716-845-1060
www.roswellpark.org/commercialization

Combinations & Methods of Use for Recombinant CD4 T Cell Receptors for Direct Tumor Recognition of Antigen

Ref# RP11-012

Keywords: CD_4^+ T helper cell, TCRα, TCRβ, NY-ESO-1, MHC class II, tumor antigen, expression vector.

Collaboration Research Opportunity: Roswell Park Cancer Institute is seeking partners to help co-develop compositions and methods for prophylaxis and/or therapy of cancers using T cells that have been engineered to be capable of direct recognition of tumor antigen and MHC class II expressing cancer cells.

Summary: CD_4^+ T cells recognize peptide fragments presented on MHC class II (HLA class II in humans). In addition to antigen-presenting cells such as macrophages and dendritic cells, many human cancer cells express MHC class II constitutively or in an IFN-γ-inducible manner although the role of MHC class II expression on human cancer cells is largely unknown.

Tumor antigen-specific CD_4^+ T helper cells play critical roles in the induction and maintenance of anti-tumor immune responses by providing "CD_4-help". Activation of CD_4^+ T cells at the local tumor sites is believed to help overcome multiple immunosuppression mechanisms and promote tumor eradication by the immune system. However, because of the frequent lack of functional antigen-presenting cells at the local tumor sites, activation of the CD_4^+ T cells and therefore the provision of CD_4^+ T help at the local tumor site is severely limited. There is accordingly, an ongoing and unmet need to provide new compositions and methods such that activation of CD_4^+ T cells and therefore provisions of CD_4^+ help can be achieved.

Technology: This invention describes sequences of TCR α and β chain genes from a novel tumor-recognizing CD_4^+ T cell clone as well as a method to prepare a large number of tumor recognizing CD_4^+ T cells by TCR gene transfer.

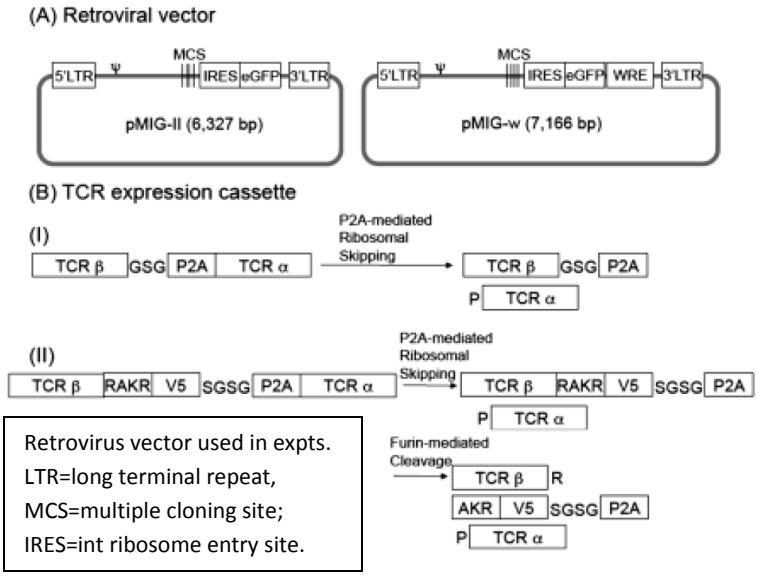
Roswell researchers have discovered that there are two distinct types of tumor antigen-specific CD4+ T cells. A part of tumor antigen-specific CD4+ T cells, that we named "tumor-recognizing CD4+ T cells (**TR-CD4**)", directly recognizes MHC class II-expressing cancer cells in antigen-specific and MHC class II-restricted manners. In contrast, other part of the same antigen-specific CD4+ T cells, "non-tumor-recognizing CD4+ T cells (**NTR-CD4**)", only recognizes the exogenous tumor antigen protein after processing by antigen-presenting cells.

Because of their different abilities in direct recognition of cancer cells, these two types of CD4+ T cells (TR-CD4 and NTR-CD4) are considered to play different roles at the local tumor site, i.e., TR-CD4 efficiently provide CD4-help by direct recognition of cancer cells.

This invention takes advantage of the fact that TR-CD4 cells provide CD4 help by direct recognition of cancer cells by using this function to provide TCR polypeptides and recombinant polynucleotides encoding them for use in novel prophylactic and/or therapeutic treatment modalities and compositions. By engineering T cells to express the TCRs researchers can endow any CD_4^+ cell with the capability to directly recognize tumor antigen-expressing cancer cells, without requiring presentation of the antigen by an antigen presenting cell. Thus, the present invention includes

ROSWELL PARK CANCER INSTITUTE

Contact:
Harl Tolbert,
techtransfer@roswellpark.org,
716-845-1060
www.roswellpark.org/commercialization



Retrovirus vector used in expts.
LTR=long terminal repeat,
MCS=multiple cloning site;
IRES=int ribosome entry site.

compositions and methods that are useful for creating and using TR-CD4 cells for improved care of cancer patients.

Potential Commercial Applications:

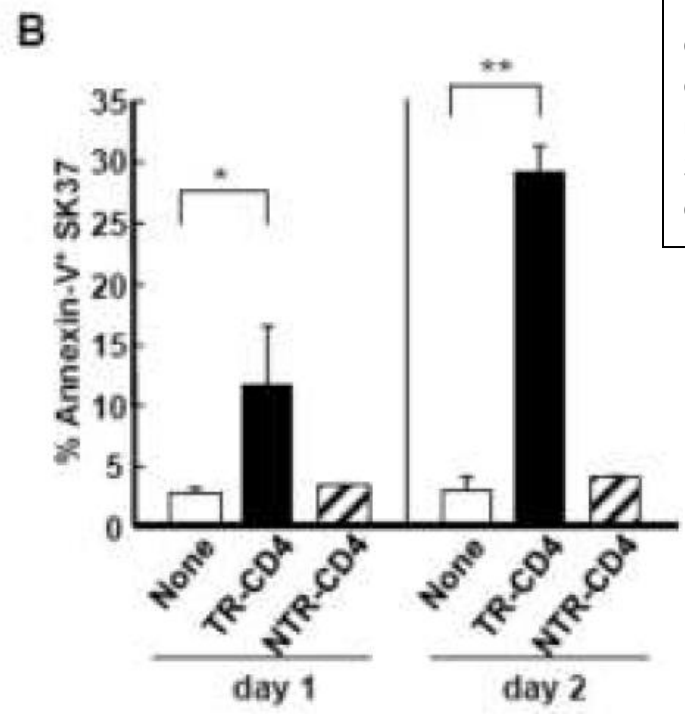
- Technology potentially provides compositions and methods for prophylaxis and/or therapy for a variety of cancers which express a NY-ESO-1 antigen.
- Technology could be useful for development of immunotherapy against cancer cells that lost MHC class I or MHC class I antigen presentation machinery.

Competitive Advantages:

- New method especially important to generate CD_4^+ T cells that provide efficient "CD4 help" at the local tumor site without the requirement of antigen presenting cells via direct recognition of cancer cells.
- Provision of "CD4 help" by current gene-engineered CD_4^+ T cells is expected to enhance the anti-tumor immune responses and overcome immunosuppression at the local tumor sites.
- TCR sequences are the first known to confer MHC class II-restricted tumor recognizing ability in humans.

Development Status: Patent Status: PCT/US14/25673 March 13, 2014

Inventor: Kunle Odunsi, MD, PhD, FRCOG, FACOG



TR-CD4 and NTR-CD4 was co-cultured with SK-MEL-37 and expression of the early apoptosis marker, Annexin-V, on SK-MEL-37 (SK37) was measured by flow cytometry.