

Extremely Rapid Method to Isolate Neoantigen Reactive T Cell Receptors (TCRs)

Summary

Researchers at the National Cancer Institute (NCI) have developed a novel method for identifying neoantigen reactive T cells and T cell receptors (TCRs), isolated from fresh tumors of common epithelial cancers. This highly specific and sensitive method allows rapid determination of the neoantigen reactive TCR sequences and can be very useful to translate this information into TCR-engineered T-cell populations for immunotherapy without the need to grow tumor infiltrating T-cells and expensive, time-consuming screening. The NCI seeks research co-development partners and/or licensees for this invention.

NIH Reference Number

E-061-2020

Product Type

- Therapeutics

Keywords

- T Cell Receptor, TCR, Tumor Infiltrating Lymphocyte, TIL, Tumor, Adoptive Cell Transfer, ACT, Immunotherapy, Neoantigen, Rosenberg

Collaboration Opportunity

This invention is available for licensing and co-development.

Contact

- Andy Burke
NCI TTC

andy.burke@nih.gov (link sends e-mail)

Description of Technology

Adoptive cell transfer (ACT) uses tumor infiltrating lymphocytes (TILs) that recognize unique antigens expressed by cancer cells (“neoantigens”). Neoantigen specific TIL administration in patients has resulted in long term regression of certain metastatic cancers. However, one of the challenges of ACT and engineered T cell receptor (TCR) therapies more broadly, is the identification and isolation of these mutation specific TILs and TCRs. Only a fraction of TILs in a given patient is known to be tumor reactive, while

the majority are not useful for cell therapy. The current procedures for isolating neoantigen reactive TILs and TCRs are time consuming, labor-intensive, and lack sensitivity and specificity.

Researchers at the National Cancer Institute (NCI) have developed a novel method to identify neoantigen reactive T cells and TCRs, isolated from fresh tumors of common epithelial cancers. This method does not require tumor cells to be grown or propagated in vitro. By using a single cell, transcriptome-based approach and barcoded antibodies (CITE-seq), neoantigen reactive T cells can be clustered within tSNE (t-Distributed Stochastic Neighbor Embedding) plots. Using genetic markers that are highly expressed in such clusters, a transcriptomic gene signature, called “NeoTCR Signature”, has been developed. This NeoTCR Signature can be used to identify a very high frequency of previously unknown T-cell clones and TCRs that recognize neoantigens from the autologous tumor. Critically, identification and isolation of the neoantigen-reactive TCR can now occur in a few days, in stark contrast to the 6-8 weeks required for current methods. This rapid determination of the neoantigen reactive TCR sequences can be useful for translating this information into TCR-engineered T-cell populations for immunotherapy. This technique can also identify T-cells with specificities for new neoantigens not presently identifiable by conventional screening methods.

NCI seeks commercial partners to co-develop and/or license this technology.

Potential Commercial Applications

- Personalized cell therapy to treat cancer patients
- Immune monitoring of other immunotherapies
- Developing treatment against chronic infections which are expected to have similar T-cell dysfunction signatures (e.g. HIV, HCV, TB, etc.)
- Research tool to identify mutation-specific TCRs
- Prognostic testing for presence of tumor-relevant TILs
- Prospective isolation of cell population ideal for introduction of stem-like factors for cell therapy
- Biomarkers in immunotherapy

Competitive Advantages

- Widely applicable to treat different types of cancer
- Significantly reduces the expensive and time-consuming procedures of tumor cell culture, propagation, and screening in vitro
- High specificity and sensitivity eliminate off-target effects
- Patient-specificity to improve efficacy of ACT or TCR therapy

Inventor(s)

[Steven Rosenberg MD, Ph.D. \(NCI\)](#), [James Yang MD \(NCI\)](#), [Ken-Ichi Handa MD, Ph.D. \(NCI\)](#), [Frank Lowery Ph.D. \(NCI\)](#), [Sri Krishna Ph.D. \(NCI\)](#), [Paul Robbins Ph.D. \(NCI\)](#), [Rami Yoseph Ph.D. \(NCI\)](#)

Development Stage

- Discovery (Lead Identification)

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/992,701 , Filed 20 Mar 2020

Related Technologies

- E-229-2014 - T-Cell Therapy Against Patient-Specific Cancer Mutations
- E-233-2014 - T-Cell Therapy Against Patient-Specific Cancer Mutations
- E-067-2017 - A Rapid Method of Isolating Neoantigen-specific T Cell Receptor Sequences

Therapeutic Area

- Cancer/Neoplasm

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