NATIONAL CANCER INSTITUTE
Technology Transfer Center

Method for Direct Identification of Neoantigen-Specific TCRs from Tumor Specimens by High-Throughput Single-Cell Sequencing

Summary

The National Cancer Institute (NCI) seeks research co-development partners and/or licensees for a method of direct identification of neoantigen-specific TCRs from tumor specimens by high-throughput single-cell sequencing.

NIH Reference Number

E-061-2021

Product Type

- Therapeutics

Keywords

- Immunotherapy, Adoptive Cell Transfer, ACT, T Cell Receptor, TCR, Single Cell Sequencing, Neoantigen, Rosenberg

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Cancer immunotherapy approaches, such as adoptive cell transfer (ACT), proved effective against many cancer types. Yet, post-treatment analyses of ACT have suggested that efficacy may be enhanced by increasing the percentage of neoantigen-reactive T cells in the infused product. Neoantigens are new proteins that form on cancer cells when certain mutations occur in tumor DNA. Current techniques for identifying neoantigen-specific TCRs in T cell expression are labor-intensive, time-consuming and technically challenging. The ineffectiveness of these techniques is a barrier against improvement of ACT and other T cell therapies. Therefore, there is a need to develop effective techniques of identifying neoantigen-specific TCRs from tumor specimens.

National Cancer Institute (NCI) scientists developed a new method of isolating neoantigen-specific TCR sequences. The method entails the isolation of tumor-infiltrating

T cells from a tumor specimen and stimulating them with neoantigen loaded dendritic cells (DCs). Isolates underwent single-cell sequencing of TCR and T-cell activation markers, IFN-γ and IL-2. This method was used to identify neoantigen-specific TCRs from three melanoma and three colorectal tumor specimens. These TCRs were then synthesized and transduced into autologous T cells, followed by testing to confirm antigen recognition. A total of 28 neoantigen-specific TCRs were identified by this process. This approach was highly reliable in identifying identical TCRs when TCR sequences were detected from two or more single cells (100%, 19 out of 19 TCRs). In summary, this single-cell approach provides an efficient process to isolate neoantigen-specific TCRs for research and clinical applications.

The NCI seeks research co-development partners and/or licensees for a method of direct identification of neoantigen-specific TCRs from tumor specimens by high-throughput single-cell sequencing.

Potential Commercial Applications

- Optimizing personalized ACT by improving the process of isolating neoantigen-specific TCRs from a patients' tumors
- Research method for identification of antigen specific TCR for scientific studies

Competitive Advantages

- Efficient, highly sensitive method of identification of neoantigen-specific TCRs from tumor specimen
- Reduces the amount of time it takes to identify neoantigen specific TCRs from tumor specimen
- Highly reliable at identifying identical TCRs isolated from multiple single cells

Inventor(s)

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Development Stage

- Pre-clinical (in vivo)

Publications

Lu YC, et al. Direct identification of neoantigen-specific TCRs from tumor specimens by high-throughput single-cell sequencing. [PMID 34321276]

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 63,148,774 , Filed 12 Feb 2021

Therapeutic Area

- Cancer/Neoplasm

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