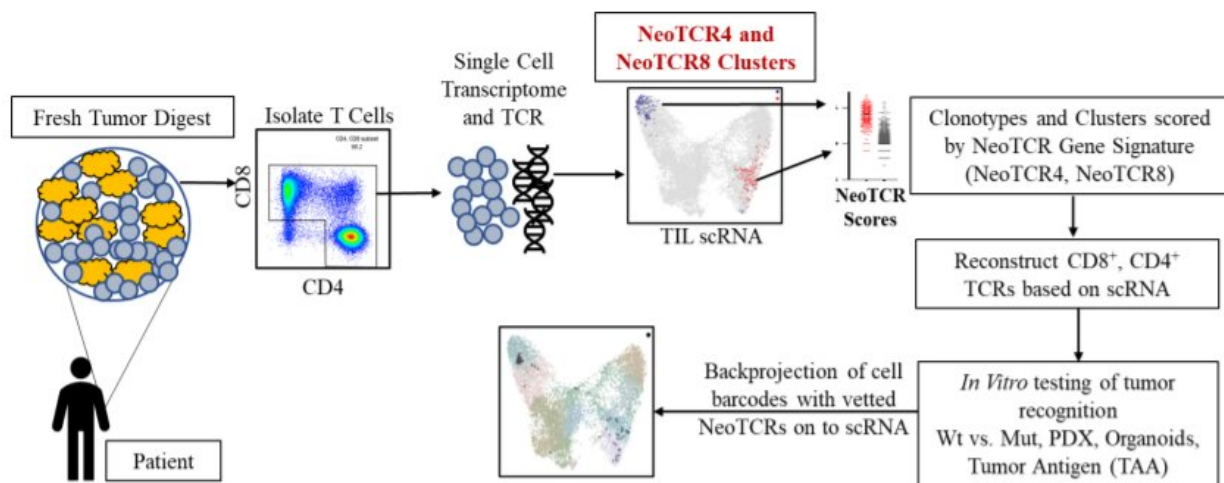


Gene expression profile allows identification of anti-tumor immune cells for personalized immunotherapy

February 4 2022



Workflow for prospective identification of anti-tumor, neoantigen-specific TCRs using NeoTCR signature. Based on single cell gene signature scoring of TIL clusters, we first identify candidate NeoTCR4 and NeoTCR8 cluster populations. Dominant and subdominant clonotypes within the the two candidate NeoTCR clusters are reconstructed and tested against autologous patient tumor mutations, overexpressed tumor antigens if reagents are available, and autologous patient tumor material (if available). Experimentally vetted NeoTCRs are backprojected on the scRNA TIL-UMAP (Fig. 3). Credit: <https://www.science.org/doi/10.1126/science.abl5447>

National Institutes of Health researchers, led by Dr. Steven Rosenberg,

MD, Ph.D., chief of the Surgery Branch at the Center for Cancer Research, National Cancer Institute (NCI), have found unique expression profiles in 50 genes that help identify rare anti-tumor lymphocytes that can infiltrate and help defeat metastatic solid epithelial tumors. To develop these profiles, a highly sensitive assay was designed that identified tumor-infiltrating lymphocytes (TIL) with cell surface receptors that can recognize the products of the very mutations that caused the cancer. The identification of these lymphocytes could help advance the development and effectiveness of personalized cancer immunotherapies for patients whose cancers do not respond to standard treatments.

This finding in TILs is especially important because it is agnostic to the type of tumor a patient has—it seems to have promise in stomach, esophageal, ovarian and breast cancers, among other types of tumors.

Until now, to maximize the potential of TIL therapy, Rosenberg's team had to look at every potential mutation in a tumor that could be a target. But after years of effort, the team developed this new assay that identifies the gene expression profiles of a few rare lymphocytes that recognize mutated cell surface proteins of cancerous cells, thereby negating the need for a mutation-by-mutation search.

Dr. Rosenberg pioneered the development of cell-based immunotherapy, a highly personalized form of cancer treatment that uses a person's own immune system to fight tumor cells. His studies of the adoptive transfer of genetically modified immune cells have resulted in tumor shrinkage in patients with metastatic cancer.

More information: Frank J. Lowery et al, Molecular signatures of antitumor neoantigen-reactive T cells from metastatic human cancers, *Science* (2022). [DOI: 10.1126/science.abl5447](https://doi.org/10.1126/science.abl5447).
www.science.org/doi/10.1126/science.abl5447

Provided by National Institutes of Health

Citation: Gene expression profile allows identification of anti-tumor immune cells for personalized immunotherapy (2022, February 4) retrieved 8 May 2024 from <https://medicalxpress.com/news/2022-02-gene-profile-identification-anti-tumor-immune.html>

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