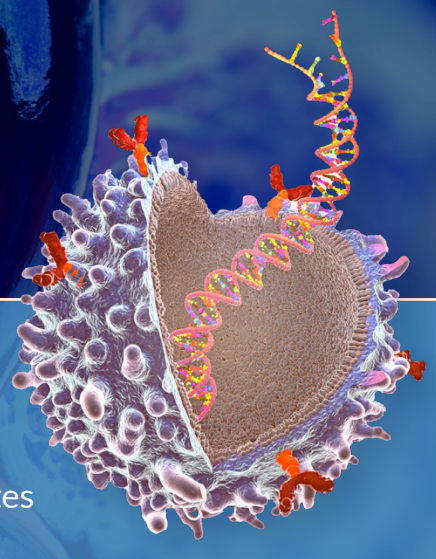
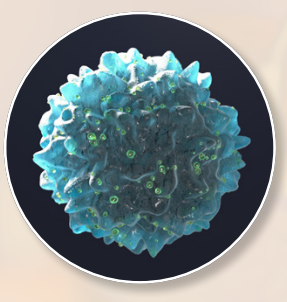
# Targeting Cancer with Adoptive Cell Therapy



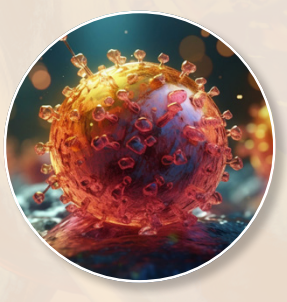
There are generally limited options for advanced or relapsed cancer. Cellular immunotherapy, also known as adoptive cell therapy (ACT), is an increasingly promising solution. ACT includes several different approaches involving tumor-infiltrating lymphocytes (TIL), genetically engineered T cell receptor (TCR), chimeric antigen receptor (CAR) modified T cells, or natural killer (NK) cells. All of these strategies have benefits and drawbacks. This infographic summarizes the various types of adoptive cell therapy, lists the advantages and disadvantages, explains why blood cancers are easier to target than solid tumors, and showcases FDA-approved and representative in-development applications.

## Types of Adoptive Cell Therapy



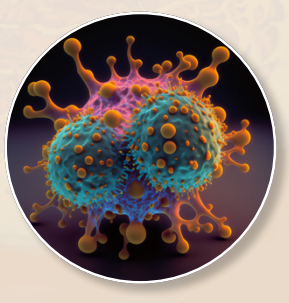
### Tumor-infiltrating lymphocyte (TIL)

Collects lymphocyte immune cells (T cells) that have already targeted the cancer, activates them, and then re-infuses them in the body.



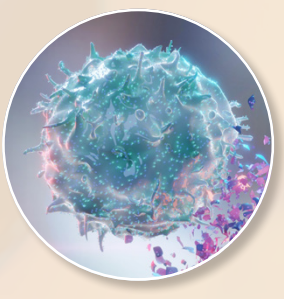
### Genetically engineered T cell receptor (TCR)

Similar to TIL therapy, but the cells are enhanced to target a specific cancer antigen.



### Chimeric antigen receptor (CAR) modified T cells

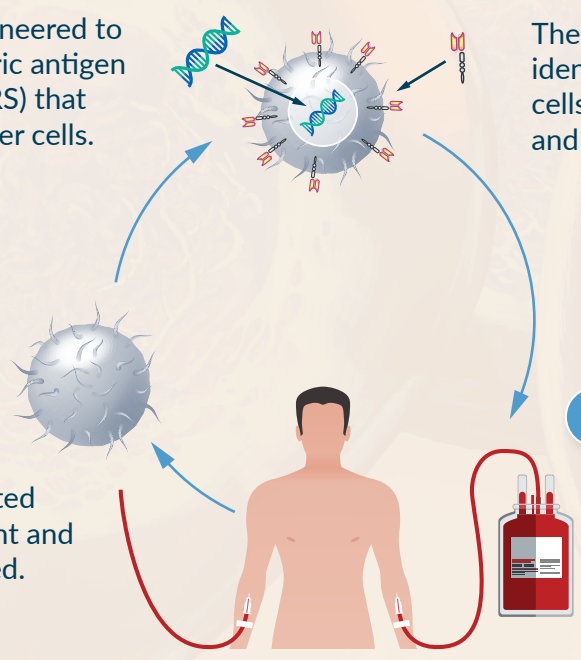
Similar to TIL therapy, but the cells are enhanced to express a recombinant receptor.



### Natural killer cells (NK)

Similar to the other three types, but uses immune cells other than T cells.

## How CAR-T works



2. T cells are engineered to express chimeric antigen receptors (CARS) that recognize cancer cells.

The engineered T cells can now identify and hone in on cancer cells, which they will latch onto and destroy.

3. Millions of CAR-T cells are grown and expanded and then infused back into patient.

1. Blood is collected from the patient and T cells extracted.

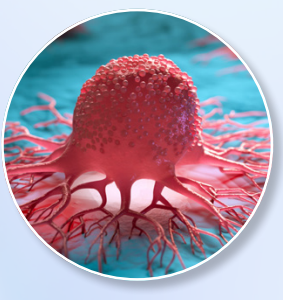
## ACT Advantages and Disadvantages

### Advantages

- Uses your body's own cells to target the cancer, and can be used in conjunction with conventional chemotherapy and radiotherapy.
- Reduced toxicities with the potential of long-term immune protection
- Short treatment time.
- Can be useful against advanced and relapsed cancer.

### Disadvantages

- There are many possible side effects, ranging from minor fatigue and speech problems to potentially fatal inflammation known as a cytokine storm.
- Therapeutic efficacy in solid tumors is limited



## Susceptible Cancers: Blood vs. Solid Tumors

Adoptive cell therapy is in principle applicable to almost any cancer. However, the challenge of expressing a clearly identifiable antigen, only in the disease of interest, with manageable off-target effects has limited approved clinical applications solely to blood cancers. Applications for solid tumors are in development.

## Approved Therapies

Among the adoptive cell therapies, CAR-T cell therapy is the only one with FDA approvals; 6 drugs are currently available for advanced or relapsed blood cancers:

### Various leukemias and/or lymphomas

- **Approved 2017:** tisagenlecleucel and axicabtagene ciloleucel
- **Approved 2020:** brexucabtagene autoleucel
- **Approved 2021**: lisocabtagene maraleucel

All target CD19, overexpressed by most B cell malignancies.

### Multiple myeloma

- **Approved 2021:** idecabtagene vicleucel
- **Approved 2022:** ciltacabtagene autoleucel

Both target B cell maturation antigen, which generally has limited expression other than in plasma cells.

## Selected In-Development Therapies for Solid Tumors

### *Gavocabtagene autoleucel—TCR Therapeutics*

Of 30 patients with mesothelioma, ovarian cancer, or cholangiocarcinoma who were evaluable afterward, 6 patients experienced a ≥30% reduction in tumor size, and 4 patients experienced tumor regression for at least 1 year. 78% of patients experienced cytokine release syndrome.

### *CRISPR-Cas9 gene editing—Penn Medicine*

In preclinical trials, disrupting two inflammatory regulators enhanced the antitumor response of CAR-T cell therapy (e.g., 10× enhanced cell replication for various solid cancer model systems, such as adenocarcinoma). As of September 2023, the FDA had not yet approved a CRISPR-Cas9 therapy for cancer.

As the science that underpins adoptive cell therapy becomes better understood, the safety and efficacy will increase. Ongoing efforts at validation in blood and solid tumors will help better meet the needs of patients with high-risk advanced and relapsed cancer.

## References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