BioLegend®
Enabling Legendary Discovery™

A Comparison of CAR-T and CAR-NK Cell Therapies

Tumor cells can progress to cancer by downregulating key molecule expression and evading immune recognition. Cell therapies use cells engineered to target specific tumors.

Chimeric antigen receptor (CAR) therapy involves the introduction of a target-recognizing molecule so that the immune cell can be activated to destroy an engaged target. $CD8^+$ T receptor cells and natural killer (NK) cells are the primary vehicles for cell therapies using CARs, referred to as CAR-T and CAR-NK respectively.

Learn how BioLegend reagents can assist with your cell therapy research:
biolegend.com/en-us/cancer

Design

1st gen. CAR T and CAR NK cells contain a surface receptor and an intracellular domain, such as a CD3ζ chain. Cellular response and cytokine release were short-lived.

2nd gen. An additional costimulatory domain, CD28 or 4-1BB, was added to allow for repeated antigen stimulation and proliferation.

3rd gen. The inclusion of a second costimulatory domain improved activation, survival, and expansion of T and NK cells.

4th gen. CAR-T: TRUCKs or T cells redirected for universal cytokine-mediated killing contain added transgenes for cytokine secretion to enhance anti-tumor activity.

CAR-NK: A unique construct containing an NKG2D ectodomain linking CD3ζ and DAP10 enhances cytotoxicity.

Cell Source

Autologous sources: Patient's peripheral blood mononuclear cells (PBMCs).

Allogenic sources: PBMCs, cell lines, stem cells from umbilical cord blood (UCB), and induced pluripotent stem cells (iPSCs).

Manufacturing

CAR Cell Manufacturing	BioLegend Research Tools
Source Cells (allogenic or autologous)	GMP RUO Flow Cytometry Antibodies
Cell Isolation and Enrichment	MojoSort™ Magnetic Cell Separation
Cell Activation or Differentiation	Bioactive Recombinant Proteins, GMP RUO Biofunctional Antibodies
CAR Gene Transfer	
Cell Expansion	Cell-Vive™ Reagents
Formulation and Cryo-preservation	
Infusion	

Therapeutic Targets

CAR-T

- CD7 (T cell acute lymphocytic leukemia)
- CD19*, CD20**, CD22 (B cell lymphoma)
- CD33 (Acute myeloid leukemia)
- CD123 (Leukemia)
- CEA (Lung, colorectal cancer)
- GD2 (Glioblastoma)
- GPC3 (Hepatocellular carcinoma)
- HER2 (Breast, Ovarian cancer)
- TNFRSF17*** (Multiple myeloma)

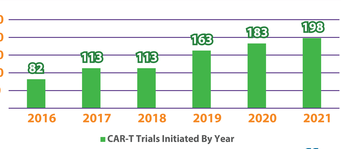
FDA-Approved Therapies
*Yescarta®, Kymriah®, Breyanzi®
**Tecartus™
***Abecma®

CAR-NK

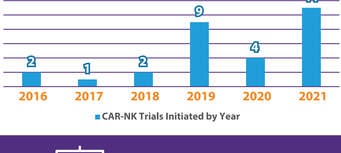
- CD19, CD22 (B cell lymphoma)
- NKG2D ligands (Leukemia and solid tumors)
- Mesothelin (Ovarian cancer)
- PSMA (Prostate cancer)
- TNFRSF17 (Multiple myeloma)

Currently, there are no FDA-approved therapies.

Clinical Trials



CAR-T Trials Initiated By Year



CAR-NK Trials Initiated by Year

Advantages

CAR-T

- Proven therapy with multiple commercial options.
- Large number of clinical trials advancing potential therapies.
- More mature therapy.
- Longer lasting than CAR-NK cells.

CAR-NK

- Superior safety with fewer side effects.
- Allogeneic NK cells can be used.
- NK cells can exert anti-tumor effects that are both CAR-dependent and CAR-independent.
- Lower cytokine release syndrome and neurotoxicity risks.
- Reduced wait times.

References:

1. Smith, Aaron J et al. "Chimeric antigen receptor (CAR) T cell therapy for malignant cancers: Summary and perspective." *Journal of Cellular Immunotherapy* vol. 2.2 (2016): 59-68. doi:10.1016/j.jocit.2016.08.001.
2. Hu, Yuan et al. "Chimeric antigen receptor (CAR)-transduced natural killer cells in tumor immunotherapy." *Acta pharmacologica Sinica* vol. 39.2 (2018): 167-176. doi:10.1038/aps.2017.125.
3. Clinical Trials Family of Sites. *National Institute of Health*, 2021, clinicaltrials.gov/. Accessed December 2021.