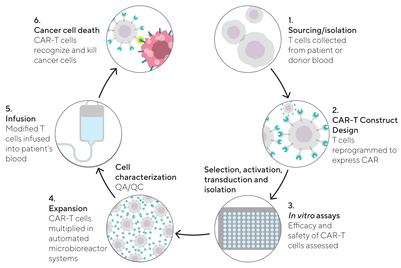
Challenges and Solutions in CAR-T Discovery and Development

Chimeric antigen receptor T cell (CAR-T) therapy is one of the key immunotherapies that is revolutionizing the landscape of medicine. The technique involves reprogramming immune cells so that they can recognize and kill cancer cells.

The complexity of CAR-T therapy yields several challenges from discovery to development. This infographic outlines the process for developing CAR-T therapies, identifies some of the critical challenges and demonstrates how solutions are overcoming these challenges – giving scientists confidence in the safety, efficacy and integrity of their next-generation CAR-T therapies.

How Does CAR-T Therapy Work?



CAR-T Therapy Discovery and Development Workflow

CAR-T Construct Design
Following isolation from patient or donor, CARs (Chimeric Antigen Receptors) are engineered to specifically target cancer cells antigens and to enchance T-Cell proliferation and cytotoxicity. Label-free Biomolecular Interaction Analysis as well as advanced flow cytometry and live-cell imaging assays provide actionable insights into these mechnisms (or into phenotyping and functional characteristics).

Activation, Transduction and *in vitro* Assays
In vitro assays are crucial for the initial research, development and characterization of CAR-T therapeutic treatments. Patient safety and time-to-result are top priorities; therefore assays need to deliver the most reproducible and biologically-relevant results.

Expansion
Part of the CAR-T discovery and development process requires cell expansion to a scale that will enable additional *in vitro* and preclinical tests, while maintaining the integrity of the cells throughout this process.

Characterization
Throughout the CAR-T therapy discovery and development process, cell characterization and safety measures must be implemented and documented thoroughly. These processes are often time-sensitive, so rapid solutions are critical. Real-time screening and analysis solutions enable continuous phenotypic and functional analysis over time, and contaminant- free systems coupled with rapid testing options help ensure safety.

Challenges in CAR-T Development

- Target antigen selection
- On-/off-target screening
- CAR delivery
- Expansion and persistence of CAR-T cells
- Contamination control

Providing Confidence in CAR-T Discovery and Development

The complexity of CAR-T cell therapy research and development, coupled with the ever-evolving nature of cancer biology, present significant challenges at different stages of the discovery and development workflow. Scientists can address these challenges using solutions that improve:

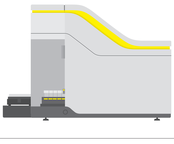
- Safety
- Speed
- Productivity
- Biologically-relevant data
- Cell characterization and QA/QC

Solutions for Each Step of the CAR-T Workflow

IncuCyte® Live-Cell Analysis Platform

Automatically capture and analyze images of living 2D and 3D cell cultures in real time with the IncuCyte® Live-Cell Analysis System.

- Sample preparation
- *In vitro* assays, selection, activation and transduction
- Characterization
- Immune cell killing



iQue® Advanced Flow Cytometry Platform

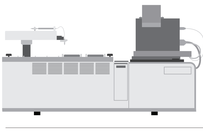
Achieve fast, reliable high-throughput analysis, using minimal sample with the iQue® Advanced Flow Cytometry Platform.

- *In vitro* assays, selection, activation and transduction
- Characterization

Octet® Label-free BLI Analysis Platform

Measure protein-protein interactions and quickly characterize expressed proteins in complex and unpurified samples in real-time.

- Affinity screening of CAR constructs
- Quantify and screen CAR-vector potency and access to target binding

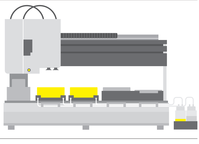


CellCelector Flex Platform

Automatically isolate clones, single cells and 3D structures with viability using CellCelector Flex.

- Isolation of successfully transduced clones and single cells
- Monoclonality assurance

Ambr® 15 Cell Culture



Achieve controlled and reproducible CAR T-cell expansion in a high-throughput, automated bioreactor system for 24 or 48 parallel cultivations at the 10 –15 mL microbioreactor scale.

- Cell expansion

Microsart® Mycoplasma and ATMP Sterile Release Kits

Ensure fast and easy contaminant detection with Microsart® real-time PCR based rapid detection kits. Detect bacterial, mycoplasma and fungal contamination within 3 hours.

- *In vitro* assays
- Expansion
- Characterization

Picus® and Tacta® Pipettes

Ensure quick and reliable liquid transfer while reducing variability between users with the multi-functional electronic Picus® and dependable manual Tacta® pipettes.

- Sample preparation
- *In vitro* assays, selection, activation & transduction
- Cell expansion
- Characterization

Learn more about Sartorius solutions for CAR-T Discovery & Development at sartorius.com/car-t-research

References
1. Srivastava, S. and Riddell, S. (2018). Chimeric Antigen Receptor T Cell Therapy: Challenges to Bench-to-Bedside Efficacy. The Journal of Immunology, [online] 200(2), pp.459-468. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5975176/ [Accessed 11 Sep. 2019].
2. Don't Compromise Your Ambition: Innovative Solutions to Advance CAR-T Discovery and Development. (2019). [PDF] Sartorius. Available at: https://www.sartorius.com/resource/blob/285374/6e4a18ab3515e8893c4006b3ca8e/broch-car-t-discovery-development-201907-data.pdf [Accessed 16 Sep. 2019].