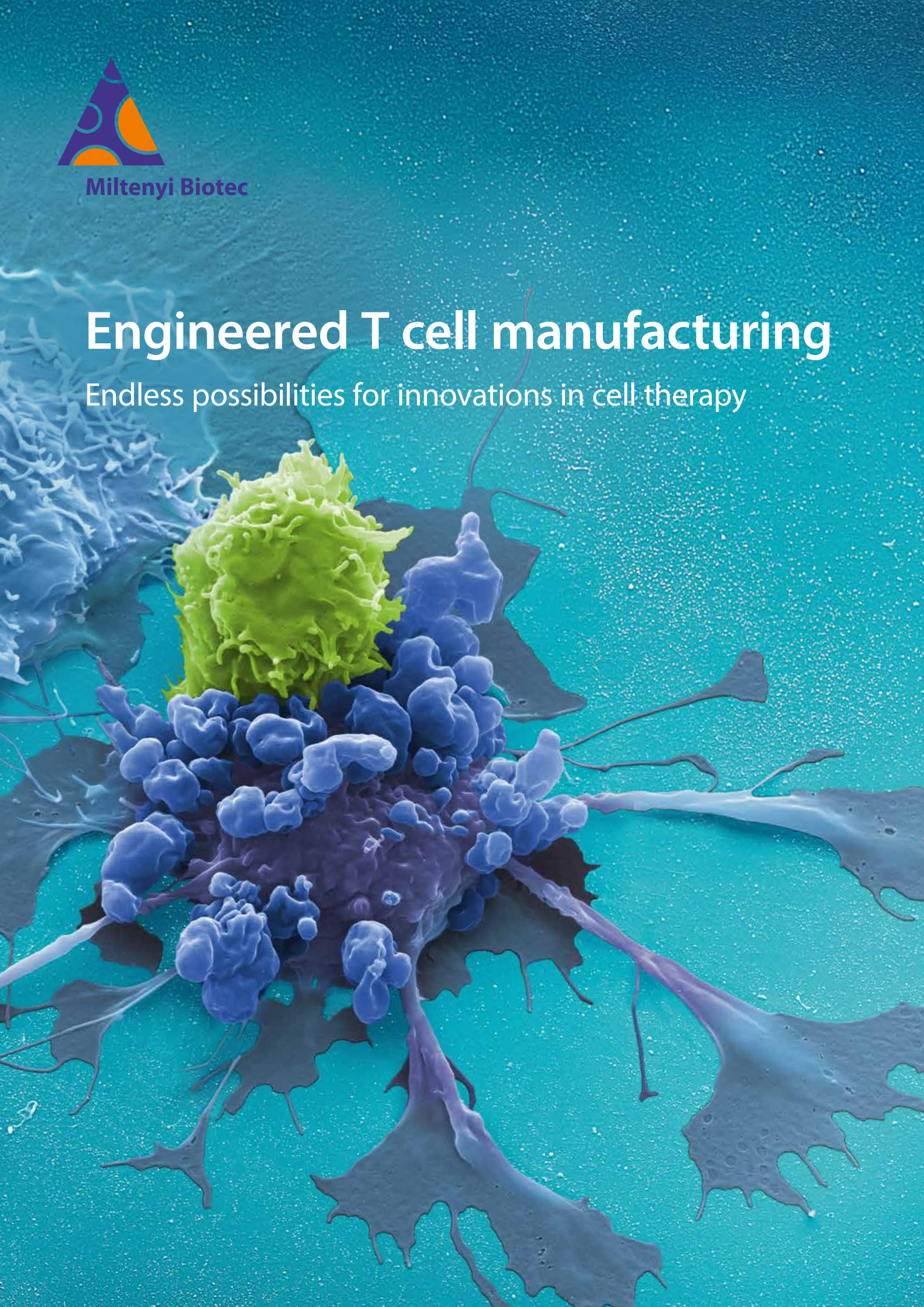
Miltenyi Biotec

Engineered T cell manufacturing

Endless possibilities for innovations in cell therapy



Flexible and customizable options for T cell therapy

Experience and success in cell manufacturing

For decades, Miltenyi Biotec has been a driving force in the development of cell manufacturing processes. In a series of instrument, reagent, and software innovations, our products and services have sparked a transition in cell processing. Time-consuming and variable manual handling is now highly standardized state-of-the-art automation.

The CliniMACS Prodigy® Platform catalyzes progress especially in T cell engineering. The instrument fosters the seamless transition of novel therapeutic strategies to clinical deployment. At the same time, it maintains a focus on consistently generating high-quality cell products.

A spectrum of options in T cell engineering

The CliniMACS Prodigy is the manufacturing platform of choice for numerous next-generation T cell therapies, including bispecific[1], switchable[2], and armored[3] CAR constructs, plus non-viral[4] and TCR engineering[5].

Three production processes underlie that diversity. The CliniMACS Prodigy T Cell Transduction (TCT) process automates efficient T cell isolation and viral transduction from a range of starting materials (Table 1). Larger volumes are managed with its large-scale counterpart, TCT–LS. Interested in electroporation for your workflow? The CliniMACS Prodigy T Cell Engineering (TCTe) process offers that option. Finally, our Customized Application Services can develop a tailored formulation and filling with the CliniMACS® Formulation Unit.

	CliniMACS Prodigy T Cell Transduction (TCT)	CliniMACS Prodigy T Cell Transduction Large Scale (TCT-LS)	CliniMACS Prodigy T Cell Engineering (TCTe)
Main manufacturing application	CAR T cells	TCR T cells and CAR T cells for solid tumors	Complex engineered T cells
Starting material			
Whole blood[6]	●		●
Buffy coat	●		●
Fresh leukapheresis	●	●	●
Frozen leukapheresis		●	
Gene engineering method			
Lentivirus/retrovirus transduction	●	●	●
Electroporation			●
Culture capacity	250 mL	600 mL	250 mL
Number of harvested cells			
Without electroporation	5×10^9	2×10^{10}	5×10^9
With electroporation			2×10^9

Table 1: Overview of the three flexible and customizable processes for T cell therapy manufacturing available on the CliniMACS Prodigy Platform.

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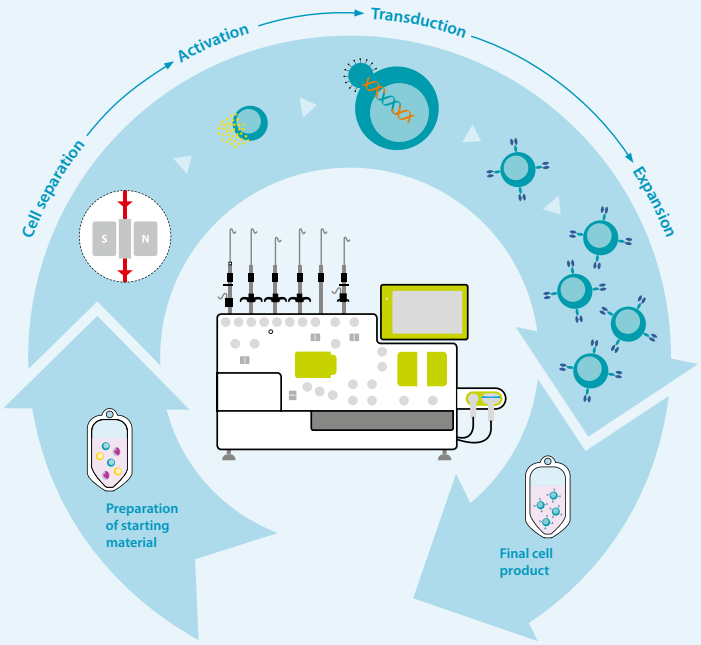
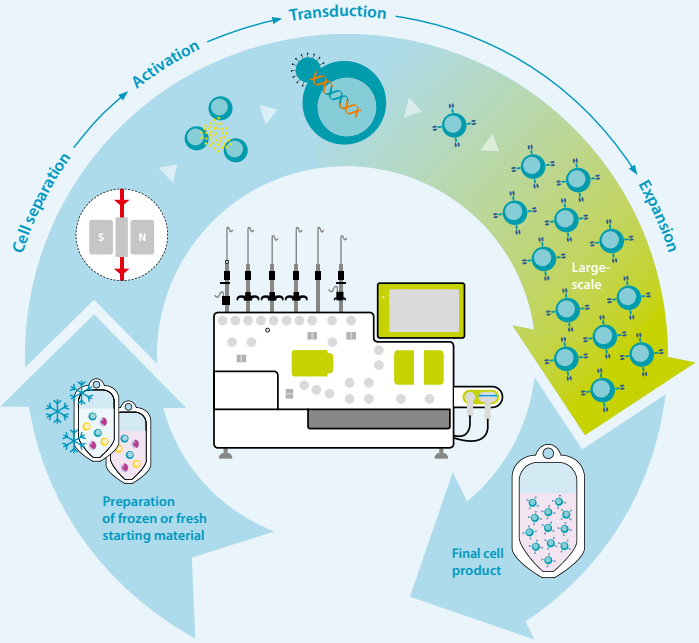
One platform. Endless possibilities.
Get an overview of our manufacturing options for gene-engineered T cells.

▸ **miltenyibiotec.com/engineeredTcells**

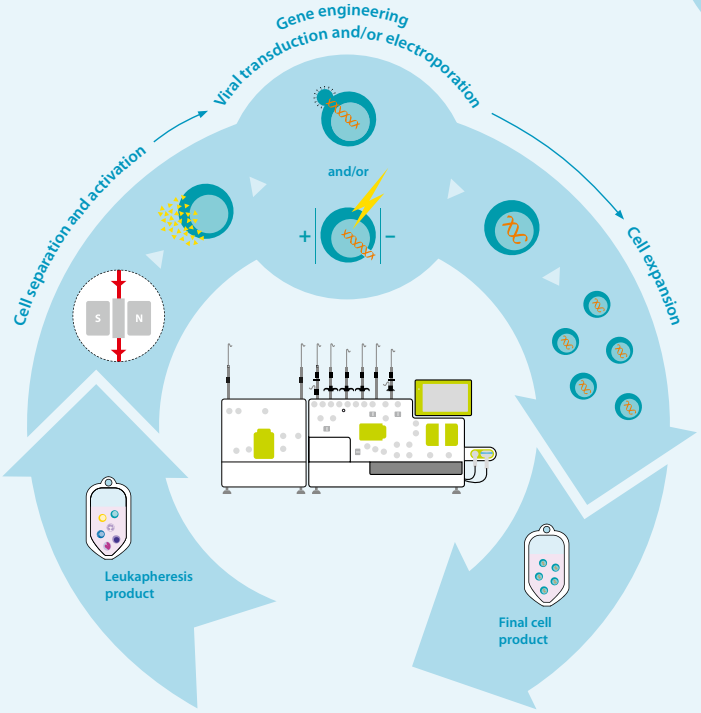
T Cell Transduction (TCT)



T Cell Transduction – Large Scale (TCT-LS)



T Cell Engineering (TCTe)



No hurdles or limits.
Just answers and options.

Integrated cell processing from collection to harvest

The CliniMACS Prodigy TCT, TCT-LS, and TCTe processes integrate optimized cell processing conditions within the protective, sterile environment of the closed CliniMACS Prodigy Platform. Each step overcomes known hurdles in T cell engineering to generate reproducible end products. Plus, automation eliminates variable material handling for standardized outcomes.

High-purity start. Reproducible results.

Effective cell manufacturing starts with a well-defined, enriched T cell population. Our three processes use clinical-scale magnetic separation to yield highly pure and viable T cells, even from patient material (internal data; fig. 1). The low monocyte content of the enriched T cells enhances transduction efficiency (fig. 2), cutting the amount and cost of vector input.

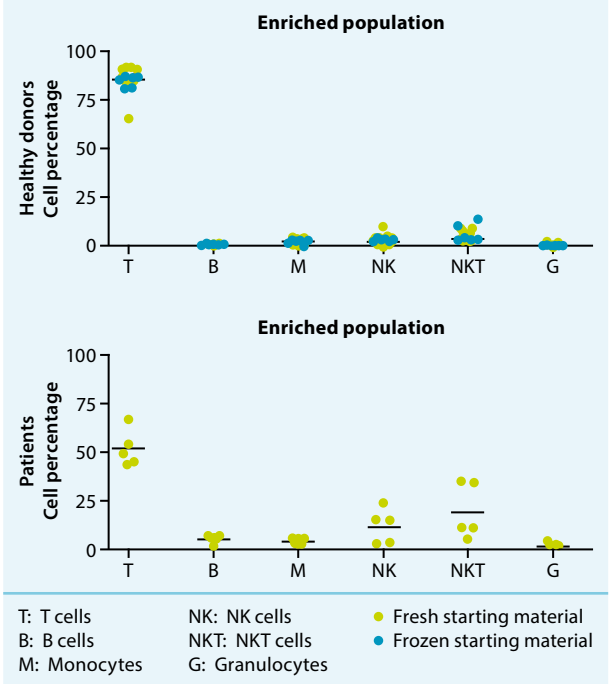


Figure 1: Automated enrichment with the CliniMACS Prodigy TCT, TCT-LS, or TCTe processes generates highly reproducible and pure T cell populations. The composition of enriched material from fresh (green) and frozen (blue) samples of healthy donors (top) and patients (bottom) is optimal for downstream steps.

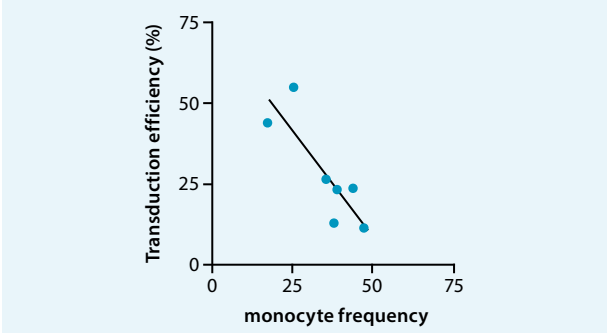


Figure 2: Unwanted cells reduce transduction efficiency significantly. A doubling in the relative proportion of monocytes in a sample lowers transduction efficiency from 50 to under 20%.

Robust and straightforward stimulation

The ready-to-use reagent MACS® GMP T Cell TransAct™ and its large-scale counterpart achieve potent polyclonal activation of cells in preparation for gene modification. Designed for use in a closed manufacturing system, MACS GMP T Cell TransAct is easy to use. Excess of the unique colloidal polymeric nanomatrix is simply washed away after stimulation.

Transduction or transfection? Your choice.

Our three T cell manufacturing processes cover lentivirus, retrovirus, and transfection-based gene modification (figs. 3 and 4). The process occurs in the closed CliniMACS Prodigy Tubing Set, ensuring safety when using viral vectors. Choose one or combine methods to efficiently perform even complex editing. The engineering step is customizable, granting full control to adapt timing, volumes, multiplicity of infection (MOI), electroporation settings, and more. Whether gene transduction, knockout, augmentation, silencing, or editing, the possibilities are endless.

Simple and convenient T cell activation

Practical application

- Volumetric dosage
- Ready-to-use
- Removal by simple washing

Robust stimulation

- Highest cell viability
- Physiological and stable stimulation

Convenient compatibility

- Available for research and GMP T cell workflows
- Optimized for CAR T cell production on the CliniMACS Prodigy
- Can be sterile filtered

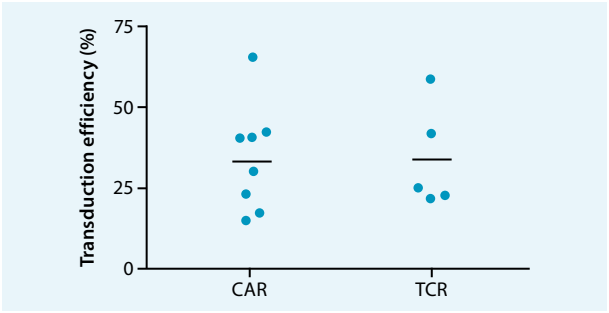


Figure 3: Enriched CD4+ and CD8+ T cells were stimulated for 24 hours before transduction using lentiviral vectors encoding CAR or TCR. The CliniMACS Prodigy TCT-LS achieved adequate and stable transduction rates.

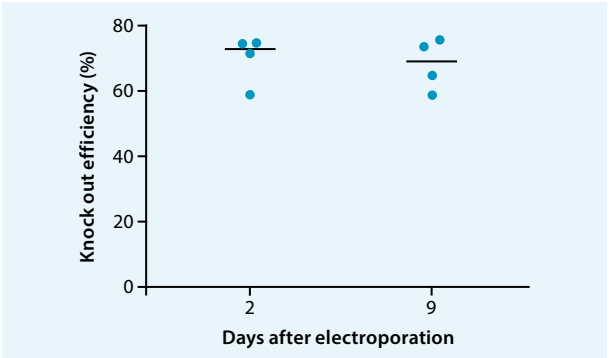


Figure 4: The gene for CCR5 was edited using transcription activator-like effector nucleases (TALENs) combined with the CliniMACS Electroporator. Editing rates at two and nine days after electroporation were comparable. Rates were calculated from gene-editing frequency digital PCR (GEF-dPCR) data (n=4).

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Simplified T cell activation
Discover the unique features of MACS GMP T Cell TransAct.
▸ **miltenyibiotec.com/GMP-TransAct**

No slowdowns or complications. Just seamless progress.

Optimal expansion to meet dosing goals

Two in-line cultivation chamber sizes house the fitting conditions to achieve standard and large-scale cell expansion (fig. 5). Each process features a ready-to-use default protocol that quickly and robustly grows the preferable T cell phenotype (fig. 6) from fresh or frozen material (fig. 7). However, cultivation parameters are programmable. Customize the culture duration, medium supply, and supernatant exchange to optimize growth or shorten manufacturing.

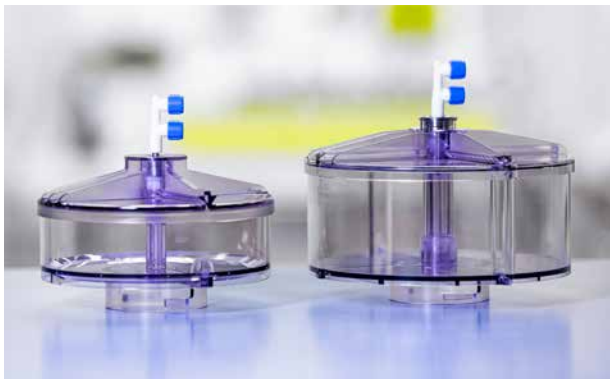

Figure 5: The CliniMACS Prodigy TCT-LS process features an expanded culture chamber (right) for large-scale production compared to the CliniMACS Prodigy TCT and TCTe (left).

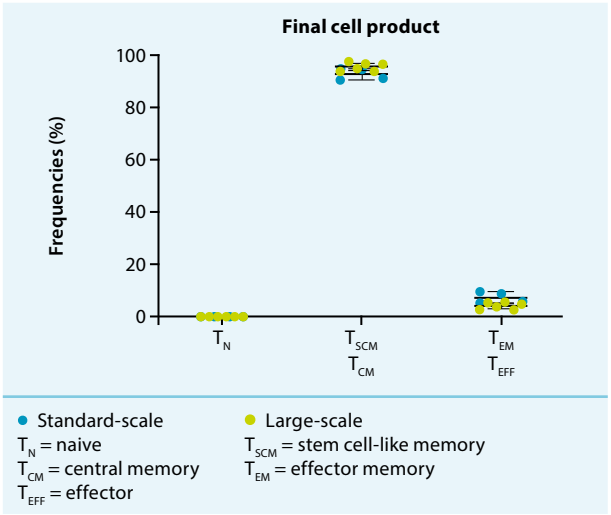

Figure 6: Frequencies of T cell phenotypes among viable CD45⁺ cells were determined for the final cell product from enriched CD4⁺/CD8⁺ T cells that were expanded in the standard and large-scale chamber of the CliniMACS Prodigy after polyclonal stimulation with MACS GMP T Cell Transact. After 12 days of culture, phenotype frequencies were comparable between the two culture conditions.

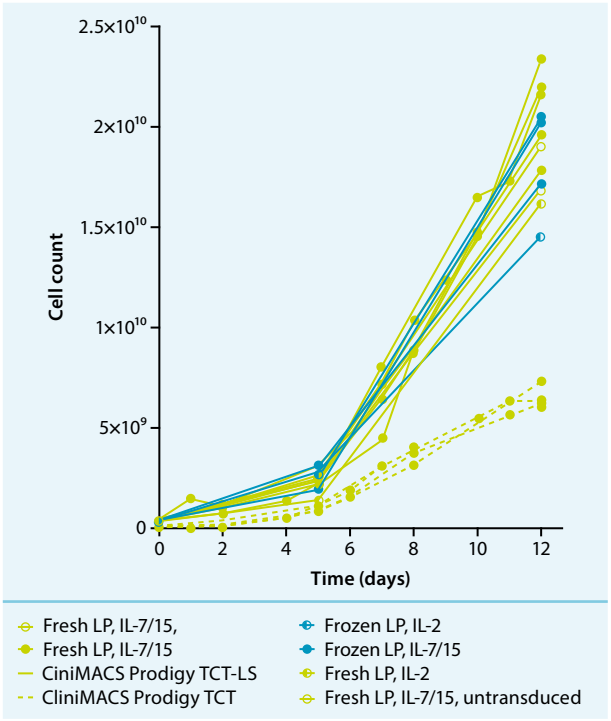

Figure 7: After polyclonal stimulation, enriched CD4⁺/CD8⁺ T cells from frozen and fresh samples were expanded in the presence of different cytokines using the standard chamber of the CliniMACS Prodigy TCT process (dotted lines) and the large-scale chamber of the CliniMACS Prodigy TCT-LS process (solid lines). Cell expansion was comparable between fresh material, frozen material, and different cytokine combinations. That consistency underscores the robustness of the process.

Aligned and reliable end-to-end IPC/RT

From in-process control (IPC) to release testing (RT), flow cytometric analysis of cell phenotype, count, function, and quality goes hand in hand with manufacturing processes on the CliniMACS Prodigy Platform. The MACSQuant® Analyzer 16, StainExpress™ dry antibody cocktails, and Express Mode software tools seamlessly interface with your production workflow and provide automated data flows for precise and consistent analyses.

150+
active clinical trials worldwide are conducted with the CliniMACS Prodigy

46+
projects in peer-reviewed articles use our clinical T cell applications

The right tools at every step

		TCT-LS (CliniMACS Prodigy Tubing Set 620)	TCT (CliniMACS Prodigy Tubing Set 520)	TCTe (CliniMACS Prodigy Tubing Set 520)
IPC/RT	Magnetic enrichment	TexMACS™ GMP Medium CliniMACS PBS/EDTA Buffer CliniMACS CD4 Product Line and CliniMACS CD8 Product Line or CliniMACS CD62L Reagent CR/GMP		
	Activation	MACS GMP TransAct – Large Scale	MACS GMP TransAct	
	Transduction/ electroporation	Lentiviral vector or gamma retroviral vector		Gene editing tools
	Cultivation	TexMACS GMP Medium MACS GMP Cytokines		
	Formulation	CliniMACS Formulation Solution		

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The perfect match
Learn how the MACSQuant Analyzers and CliniMACS Prodigy were made for one another.
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Read other clinical research papers that reference the CliniMACS Prodigy.
▸ **miltenyibiotec.com/Tcell-engineering-refs**

References

1. Shah, N. N. *et al.* (2020) Nat. Med. 26: 1569–1575.
2. Loff, S. *et al.* (2020) Mol. Ther. Oncolytics 17: 408–420.
3. Glienke, W. *et al.* (2022) Front. Immunol. 13: 839783.
4. Lock, D. *et al.* (2022) J. Immunother. Cancer 10: e005189.
5. Foy, S. *et al.* (2023) Nature 615: 687–696.
6. Lock, D. *et al.* (2017) Hum. Gene Ther. 28: 914–925.

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