



Miltényi Biotec

The CliniMACS Prodigy® HSC Engineering process



CliniMACS Prodigy HSC Engineering process

Reliable and safe engineering of
hematopoietic stem cells. Today.



Automated



Robust



Flexible



Functionally
closed system

Overview

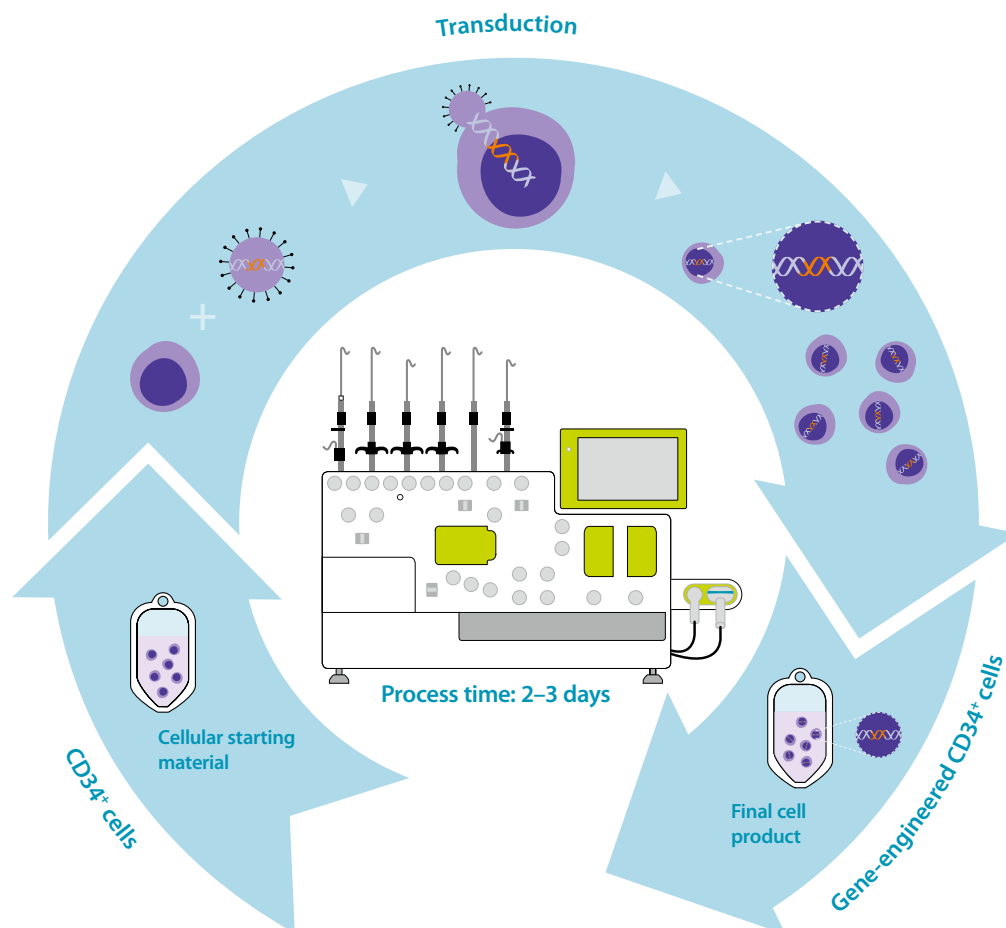


Figure 1: Overview of the CliniMACS Prodigy HSC Engineering process. Day 0, connect your cell bag containing enriched CD34⁺ cells to the CliniMACS Prodigy Tubing Set (TS) 520 installed on the CliniMACS Prodigy Instrument. After pre-cultivation in HSC-Brew GMP Medium supplemented with cytokines within the chamber, cells can be transduced on day 1 and additionally on day 2 if two transduction rounds are needed (further transduction rounds can also be executed if required). Gene-engineered HSCs can be harvested on day 2 or 3, respectively.

Specifications

Cellular starting material:	CD34 ⁺ cells, e.g., enriched from mobilized leukapheresis
Starting cell number:	at least 2×10^7 cells
Starting sample volume:	40–250 mL
Final product:	gene-engineered CD34 ⁺ cells
Final product volume:	100 mL
Process time:	2–3 days
Hands-on time:	approx. 2 hours

Viral transduction of CD34⁺ cells is a promising approach to understand inherited disorders, such as sickle cell disease, β -thalassemia, or primary immunodeficiencies.^{1–3} The CliniMACS Prodigy HSC Engineering process allows for the manufacturing of gene-engineered hematopoietic stem cells (HSCs) from human CD34⁺ cells, e.g., from mobilized leukapheresis. All manufacturing steps take place in the functionally closed, sterile, and single-use tubing set, ensuring safe manufacturing and cell products.

LEARN MORE



The CliniMACS Prodigy can generate CD34⁺-enriched cells with up to 95% purity. Visit us to learn more.
► miltenyibiotec.com/CD34-cell-enrichment

IPC/QC and performance

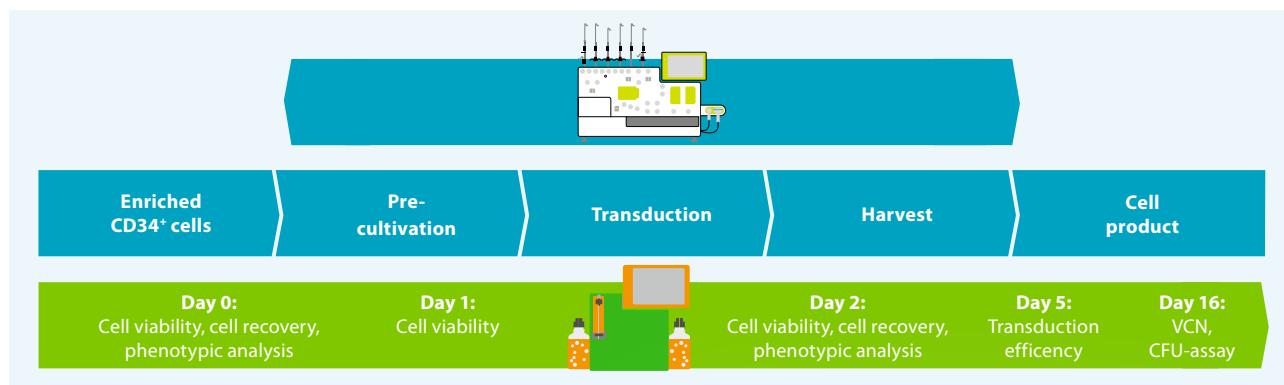


Figure 2: Overview of the IPC/QC timeline of gene-engineered HSCs. For IPC, cell viability over time and recovery are investigated on days 1–2. For QC, the functionality of the gene-engineered HSCs is analyzed by phenotypic analysis of CD34, CD90, and by colony-forming unit (CFU) assays. Furthermore, the efficiency of the viral transduction is studied by the transduction efficiency and vector copy number (VCN).

In-process and quality control (IPC/QC) are required for consistent cell manufacturing of gene-engineered HSCs. Integrated sampling pouches on the CliniMACS Prodigy TS 520 allow for controls to be collected at any time throughout the cell manufacturing process. In addition, with the MACSQuant® Flow Cytometers and a wide portfolio of MACS® Antibodies, Miltenyi Biotec provides complete solutions for IPC/QC of gene-engineered HSCs.

The CliniMACS Prodigy HSC Engineering process results in a more consistent recovery of viable CD34⁺ cells compared to manual processing (fig. 3). This generates higher transduction rates at low, non-saturating multiplicity of infections (MOIs) for the lentiviral transduction of human CD34⁺ cells with GFP vector (fig. 4).

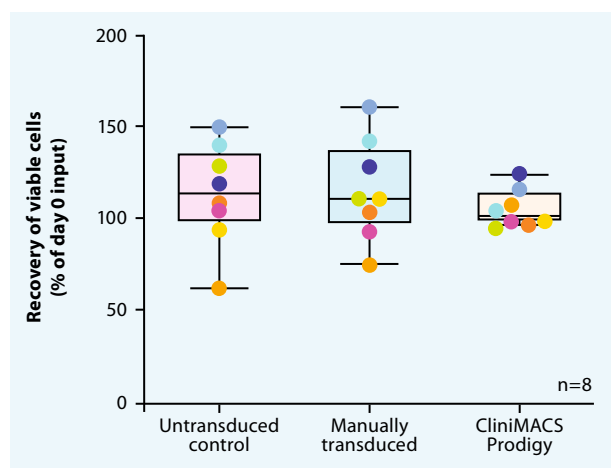


Figure 3: Cell recovery of viable cells on day 2 related to the number of viable cells measured on day 0 as set to 100%.

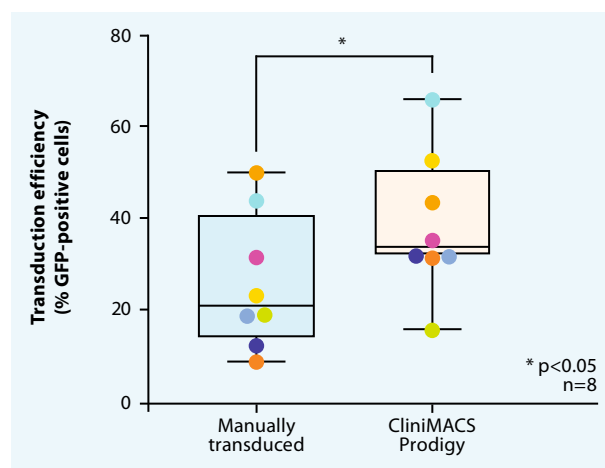


Figure 4: Transduction efficiency of viable CD34⁺CD45⁺ cells detected on day 5 by flow cytometric measurement of GFP⁺ cells.

LEARN MORE



Check out how to conduct IPC/QC with our application note!

► miltenyibiotec.com/HSC_IPC_QC

Training and resources

CliniMACS Prodigy HSC Engineering process user training

This two-day training offers an application-specific introduction to the HSC Engineering process on the CliniMACS Prodigy Instrument. During the training, all process steps including culture set up, transduction, cultivation, and harvest are explained and demonstrated to provide an extensive hands-on understanding of the versatility of the process.

Further questions?

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Browse through our clinical cell manufacturing training courses!

► miltenyibiotec.com/clinical-cell-manufacturing-training-courses

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Product List

Products	Order no.
CliniMACS Prodigy Instrument	200-075-301
CliniMACS Prodigy TS 520	170-076-600
HSC-Brew GMP Medium	170-076-310
MACS GMP Recombinant Human Flt3-Ligand	170-076-132
MACS GMP Recombinant Human SCF	170-076-133
MACS GMP Recombinant Human TPO	170-076-134
MACS GMP Recombinant Human IL-3	170-076-110
MACSQuant Analyzer 10	130-096-343
CD34 Antibody, anti-human, PE-Vio® 770	130-113-180
CD45 Antibody, anti-human, VioBlue®	130-113-122
CD90 Antibody, anti-human, APC, REAfinity™	130-114-861
StemMACS™ HSC-CFU Assay Kit, human	130-125-042

References

1. de Dreuzy E. *et al.* (2016) Current and future alternative therapies for beta-thalassemia major. *Biomed. J.* 39: 24–38.
2. Lebensburger, J. and Persons D. A. (2008) Progress toward safe and effective gene therapy for beta-thalassemia and sickle cell disease. *Curr. Opin. Drug Discov. Devel.* 11: 225–232.
3. Papanikolaou E. and Anagnou N. P. (2010) Major challenges for gene therapy of thalassemia and sickle cell disease. *Curr. Gene Ther.* 10: 404–412.

RESOURCES



Master the complexity of cell processing with a CliniMACS Prodigy introduction.

► miltenyibiotec.com/prodigyintroduction



View the HSC Engineering process in action!

► miltenyibiotec.com/HSCEvideo



Take a look at the manual vs. automated process comparison data.

► miltenyibiotec.com/HSCautomatedmanual



Learn more about the HSC Engineering process with our webinar.

► miltenyibiotec.com/HSCEwebinar



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In the EU, the CliniMACS System components are available as CE-marked medical devices for their respective intended use, unless otherwise stated. The CliniMACS Reagents and Biotin Conjugates are intended for *in vitro* use only and are not designated for therapeutic use or direct infusion into patients. The CliniMACS Reagents in combination with the CliniMACS System are intended to separate human cells. Miltenyi Biotec as the manufacturer of the CliniMACS System does not give any recommendations regarding the use of separated cells for therapeutic purposes and does not make any claims regarding a clinical benefit. For the manufacturing and use of target cells in humans, the national legislation and regulations – e.g. for the EU the Directive 2004/23/EC ("human tissues and cells"), or the Directive 2002/98/EC ("human blood and blood components") – must be followed. Thus, any clinical application of the target cells is exclusively within the responsibility of the user of a CliniMACS System.

In the US, the CliniMACS CD34 Reagent System, including the CliniMACS Plus Instrument, CliniMACS CD34 Reagent, CliniMACS Tubing Sets TS and LS, and the CliniMACS PBS/EDTA Buffer, is FDA approved as a Humanitarian Use Device (HUD), authorized by U.S. Federal law for use in the treatment of patients with acute myeloid leukemia (AML) in first complete remission. The effectiveness of the device for this indication has not been demonstrated. Other products of the CliniMACS Product Line are available for use only under an approved Investigational New Drug (IND) application, Investigational Device Exemption (IDE) or FDA approval.

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