The CliniMACS Prodigy®: An adaptable, intelligent centerpiece for customizable manufacturing strategies

Introduction

The customization imperative

The transition of cell therapy from a revolutionary breakthrough to an established treatment pillar has placed immense pressure on manufacturing infrastructures. As therapy designs evolve toward larger patient populations and autoimmune indications, achieving greater manufacturing throughput requires platform flexibility. Whether a cell therapy manufacturer is focusing on parallel autologous manufacturing or high-yield allogeneic "off-the-shelf" modalities — which leverage healthy donor material to produce hundreds of doses — the manufacturing platform must adapt to larger volumes and unconventional workflows without compromising the integrity of a closed system.

Orchestrating flexibility: The CliniMACS Prodigy as an intelligent hub

The CliniMACS Prodigy is the established industry workhorse for end-to-end automated cell processing. While features like its internal large-scale cultivation chamber provide a robust environment for many clinical applications, additional capabilities are available via its open architecture. Rather than being a "fixed-process" instrument, the CliniMACS Prodigy serves as an intelligent hub capable of integrating auxiliary cultivation chambers to meet the ever-evolving needs of therapy developers.

This expanded repertoire is made possible through intrinsic hardware features and customizable workflows, including the integration of external culture vessels such as the G-Rex® bioreactor (Wilson Wolf Manufacturing). Using sterile welding and bespoke fluid-path programming, the CliniMACS Prodigy orchestrates liquid handling for external devices within a functionally closed system.

This inherent flexibility allows manufacturers to:

1. **Scale vertically** and transition to larger volumes for allogeneic batches that exceed standard internal capacities.
2. **Scale horizontally** to maximize instrument return on investment (ROI). By offloading the expansion phase — the longest stage of the 7-to-10-day manufacturing cycle — to an external vessel, the CliniMACS Prodigy is free to begin a new enrichment and transduction run for a subsequent batch.
3. **Maintain absolute sterility** with all volume additions, media exchanges, and harvests occuring through a sealed, GMP-compliant tubing set.

Custom applications: tailored to your pipeline

At the heart of this flexibility is the Miltenyi Biotec Applications Development team. Innovation requires specialized solutions and our custom applications (CAPs) experts from the Applications Development team collaborate directly with therapy developers to program specific workflows, allowing the CliniMACS Prodigy to automate complex liquid handling for various external vessels.

These workflows include the precise addition and removal of media, cytokine supplementation, and automated harvest — transforming what were once manual and labor-intensive steps into a seamless, reproducible, and automated program.

Expert insight from the Applications Development team: "The CliniMACS Prodigy was engineered to bridge the gap between standard automation and unique process requirements. Through our unique program development service (CAPs), we empower the platform to adapt to your specific workflow rather than forcing you to compromise your science. Whether you are integrating specialized expansion vessels or designing complex parallel-processing schedules to maximize throughput, the CliniMACS Prodigy provides the versatility needed to optimize manufacturing your way. This adaptability is precisely why the platform remains the gold standard from the bench to commercial scale."

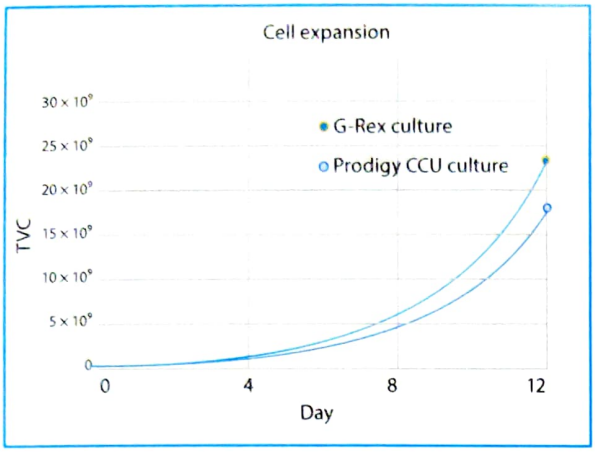

Figure 1: Total viable cell (TVC) expansion in the G-Rex 500M-CS is comparable to TVC expansion in the CliniMACS Prodigy CentriCult Unit (CCU).

Case study: Integration of the CliniMACS Prodigy and external bioreactors to generate CAR T cells

A common industry misconception suggests that the CliniMACS Prodigy and third-party expansion technologies, such as the G-Rex bioreactor, are independent, incompatible systems. In reality, our data demonstrates they are highly complementary when the CliniMACS Prodigy is utilized as the primary controller.

The protocol:
In this study, the T cell transduction-large scale (TCT-LS) standard process was used to manufacture CD19/CD20 CAR T cells.

1. **Initiation:** On Day 0, T cells were enriched, activated with MACS® GMP T Cell TransAct™, and transduced **using a CliniMACS Prodigy Tubing Set 620.**
2. **Transfer:** On Day 5, the cells were washed in fresh TexMACS™ GMP Media and transferred into G-Rex 500M-CS devices (filled to 5L) using the harvest modules within the TCT-LS standard program.
3. **Automated harvest:** On Day 12, a CliniMACS Prodigy CAP was used in combination with a CliniMACS Prodigy Tubing Set 720. The program created a constant overpressure in the G-Rex, allowing for the automated removal of 80% of the media through the supernatant line.
4. **Collection:** The remaining 1L of culture was automatically harvested into the CentriCult™ Unit (CCU) of the CliniMACS Prodigy Tubing Set 720, washed in formulation solution, and eluted for cryopreservation.

Results: high yields and superior phenotypes.

The CliniMACS Prodigy and G-Rex integration yielded large cell numbers with high frequencies of naïve and central memory phenotypes: 85.8% for $CD4^+$ and 93.5% for $CD8^+$. These proportions closely mirrored the CliniMACS Prodigy CCU control culture (88.5% and 93.2%, respectively) and are critical for ensuring sustained persistence in clinical applications. Functionally, both platforms produced CAR T cells with potent effector function, achieving >90% target cell killing at a 10:1 E:T ratio after 48 hours.

Parameter	Result
Expansion rate	Comparable to internal standards
Phenotype	**Dominated by naïve and central memory T cell phenotypes**
Cytotoxicity	Robust killing of Raji B cell lymphoma targets
System integrity	**100% sterile, functionally closed workflow**

Ultimately, these results showcase the versatility of the CliniMACS Prodigy in managing sophisticated, third-party expansion technologies. This integrated approach successfully automates complex liquid handling and harvest protocols, ensuring that high standards for product quality are maintained throughout a streamlined, closed-system process.

Conclusion: a future-proof platform

The CliniMACS Prodigy is more than a standalone instrument, it is an adaptable ecosystem that serves as the intelligent centerpiece for customizable manufacturing strategies. By combining the innovative system's automated precision with the specialized expansion capabilities of external vessels — all orchestrated by our CAP experts from the Applications Development team — manufacturers can achieve unprecedented throughput.

This hybrid approach allows for parallel runs that maximize hardware ROI while providing the volume flexibility required for the next generation of cell therapies. As the cell and gene therapy landscape evolves, Miltenyi Biotec remains committed to providing the versatile tools necessary to make life-saving treatments a reality for patients worldwide.

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