Case Study

From R&D to GMP: Successful Clinical-Grade Manufacturing of an NK Cell Therapy

Context and Challenge

Cell Easy's client, a European biotech working on an **allogeneic NK cell immunotherapy**, had initially developed their process in an **academic research** setting suitable for small-scale R&D and exploratory work. However, it lacked robustness, reproducibility, and regulatory rigor required for **clinical trials.** The company's key objective was to adapt and **scale up** their process under **GMP conditions** to support a **First-in-Human (FIH) clinical trial**. The final product needed to meet strict quality attributes such as safety, potency, and stability without compromising the unique biological properties of NK cells.

Our Approach

1 Ex Vivo expansion of NK Cells

Challenge: **NK cells** are known for their inherent **biological complexity** and relatively **low proliferative capacity** compared to other immune cell types like T cells. Achieving their **expansion** without loss of **cytotoxic function** posed significant challenges due to the risk of **cell exhaustion** under GMP conditions, where process flexibility is limited and culture durations tend to be longer.

Our solution: We **optimized media composition** and **feeding schedules** to maintain ideal cytokine and nutrient levels, carefully **calibrated feeder cell ratios** and **seeding densities** to enhance expansion while minimizing exhaustion and implemented **strategic timing for interventions** to preserve NK cell phenotype and maximize overall yield.

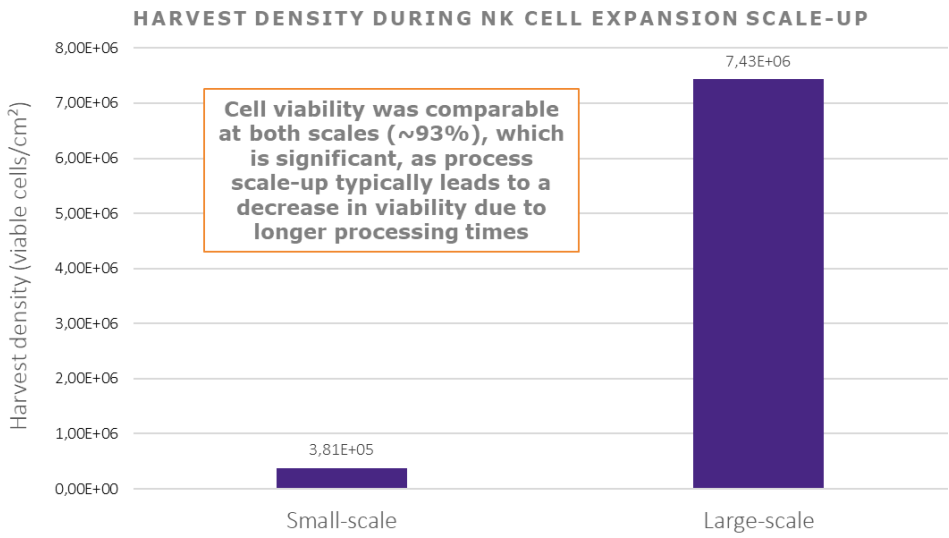

Fig 1: Harvest Density During NK Cell Expansion Scale-up – Cell Easy

2 Feeder Cell Process Development

Challenge: Scaling a **feeder-dependent process** to **GMP manufacturing** required the creation of both a **Master** and a **Working Cell Bank** for **feeder cells**. This had to be done while addressing key challenges: limited **feeder cell availability**, the limitations of **small-scale academic protocols**, and the operational complexity of maintaining **consistency at large scale**.

Our solution: We **scaled up from small culture formats to large bioreactors** and implemented a **two-tier expansion strategy with an intermediate feeder cell bank**, increasing feeder cell quantity **sixfold**. This significantly improved **cost-efficiency** and **process consistency**.

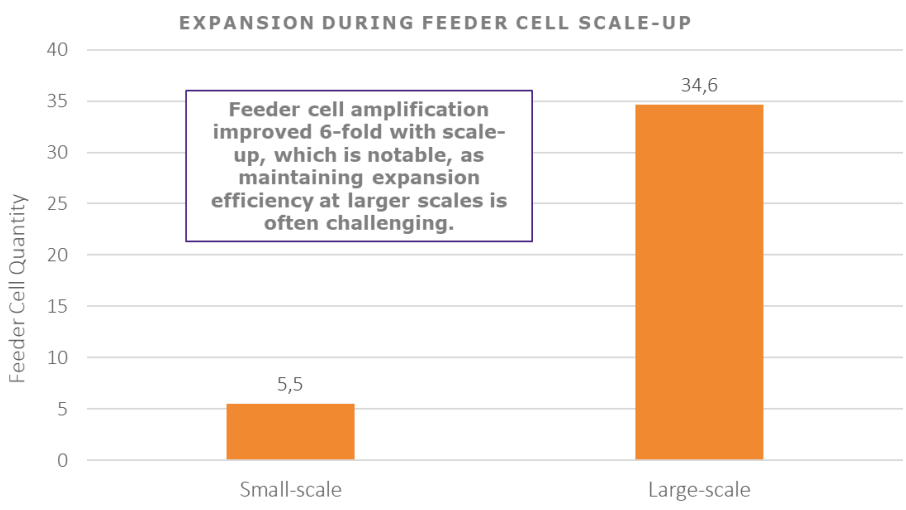

Fig 2: Fold Expansion during Feeder Cell Scale-Up– Cell Easy

3 Cryopreservation and Stability

Challenge: A critical requirement for the client's allogeneic NK therapy was maintaining **NK cell viability and cytotoxic activity following cryopreservation at −150 °C.** This is particularly challenging due to the cells' high sensitivity to **osmotic stress**, **limitations of** commonly used **cryoprotectants**, and the **risk of intracellular ice formation** during freezing, all of which can compromise product quality upon thawing.

Our solution: We established a **controlled-rate freezing protocol** designed to **minimize intracellular ice formation**, safeguarding **cell integrity** during cryopreservation. A **custom cryoprotectant** formulation was developed and optimized for **NK cell preservation**, improving **post-thaw viability** and **potency**. In parallel, we standardized **thawing procedures** to ensure **reproducible recovery** and consistent functional performance across clinical sites, supporting product deployment in multicenter trials.

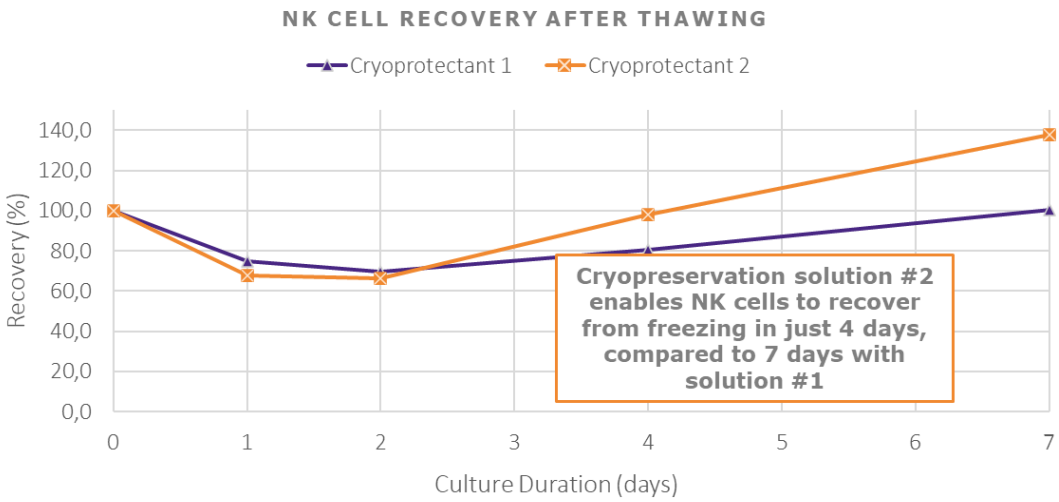

Fig 3: NK Cell Recovery After Thawing– Cell Easy

4 GMP-Compliant Sourcing and Regulatory Strategy

Challenge: Bringing this NK cell therapy from **early-stage development** to **clinical readiness** required overcoming multiple hurdles simultaneously: securing a **reliable supply** of **GMP-grade starting material,** ensuring **full traceability,** and **navigating complex regulatory** and **CMC requirements**—all while adapting the process to a new scale and maintaining product quality.

Our solution: Cell-Easy delivered an **integrated approach** combining **supply chain reliability with expert regulatory** and **CMC support**. This included sourcing **GMP-compliant cord blood** through trusted **European partners**, embedding **quality** and **traceability** into the supply process, qualifying **key subcontractors**, conducting **preclinical toxicology studies**, managing **regulatory interactions with ANSM**, and finalizing the **IMPD**.

Sourcing & Traceability

- EU network of public & private cord blood banks
- Integrated into Cell-Easy's QMS
- Full donor screening (HLA, viral, counts)

Regulatory Execution

- Preclinical toxicology study (ICH-compliant)
- Scientific advice with ANSM
- IMPD authored and submitted

Results and outcome

Over a **28-month collaboration**, Cell-Easy successfully transformed a **research-stage NK cell** program into a **GMP-compliant manufacturing process** ready **for clinical application**. This achievement included the production and qualified release of **one GMP engineering batch and two GMP clinical batches**—each meeting all predefined quality and release specifications.

By integrating **process development** with rigorous **quality assurance** and **regulatory oversight**, we ensured full alignment with **European GMP standards** throughout the project lifecycle. These coordinated efforts culminated in the successful submission and approval of **the client's Clinical Trial Application (CTA),** enabling the initiation of **Phase 1 patient dosing**. This milestone marks a significant step toward bringing a novel **NK cell therapy to patients**.

Complete process redevelopment

From academic R&D to GMP-compliant scale-up

3 GMP batches produced and released

One engineering and two clinical batches

Integrated quality and regulatory workflows

Ensuring full compliance with European regulations

Clinical Trial Application approved

Authorizing initiation of Phase 1 patient dosing

Conclusion

This collaboration illustrates Cell-Easy's capacity to deliver comprehensive, **GMP-compliant solutions** for complex **cell therapy products**. From **feeder-based process development** to **regulatory approval**, we provided a seamless **end-to-end service** enabling **clinical translation**.

As a specialized CDMO in cell therapies, Cell-Easy accelerates product development by combining deep **scientific expertise**, **GMP manufacturing capabilities**, and **regulatory insight**. Whether your program is in early discovery or near clinical transition, we are ready to be your trusted partner in bringing advanced therapies to life.

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