

# ELECTA™ producer cell line

## GENE THERAPY TECHNOLOGY

Delivering on the promise of AAV-based gene therapies beyond rare diseases will require large quantities of high-quality AAV, produced in a robust manner.

ELECTA™ producer cell line is a stable cell line for inducible AAV production. It is a true producer cell line that has Rep, Helper, Cap, and gene of interest (GOI) stably integrated into the host cell's genome, and requires only a single induction step to initiate AAV production.

The ELECTA producer cell line offers the following benefits:

- **Simplified manufacturing process:** Replace multi-step transfection with single-step production by adding an induction reagent.
- **Scalability:** Scale up seamlessly to achieve large quantities of AAV material.
- **Reproducibility:** Benefit from a monoclonal cell line from which AAV is produced in an identical manner, enabling consistency from batch to batch.
- **Reduced COGS:** Skip the need for large quantities of transfection reagent and any plasmid DNA, which are the most expensive raw materials in classical AAV transient transfection.

## Development of ELECTA producer cell line

Figure 1 shows an overview of the ELECTA producer cell line development process. It is tailored using client-specific capsid and GOI transgenes that are stably integrated into the ELECTA alpha cell line. Cytiva offers two ELECTA alpha cell lines — modified clonal HEK293 or a cell line derived from human amniocytes (CAP™ cell line from Cytiva). Both alpha cell lines have Rep and Helper functions already stably integrated into their genome.

We use cloning and high-throughput screening technologies for single-cell cloning of the producer pool, from which we then select the best producer single-cell clones that give high titers and high full/empty ratios. A research cell bank is then generated and transferred to the client. We provide an optional service to optimize process development, if desired, prior to generating the research cell bank.

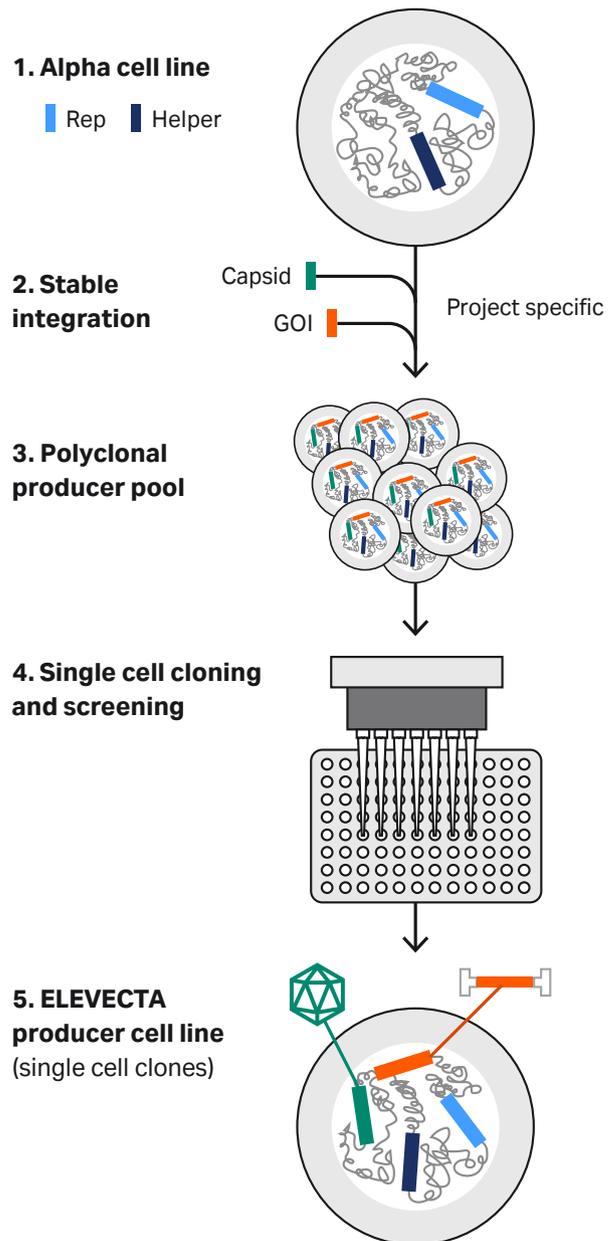


Fig 1. ELECTA producer cell line development process.

## Simplified manufacturing process of AAV

Limitations of transient transfection are inherent to the complexity of the method, because multiple manual steps must be performed for every batch. A stable ELEVECTA producer cell line simplifies production processes to save on production time, enhance quality, and reduce COGS.

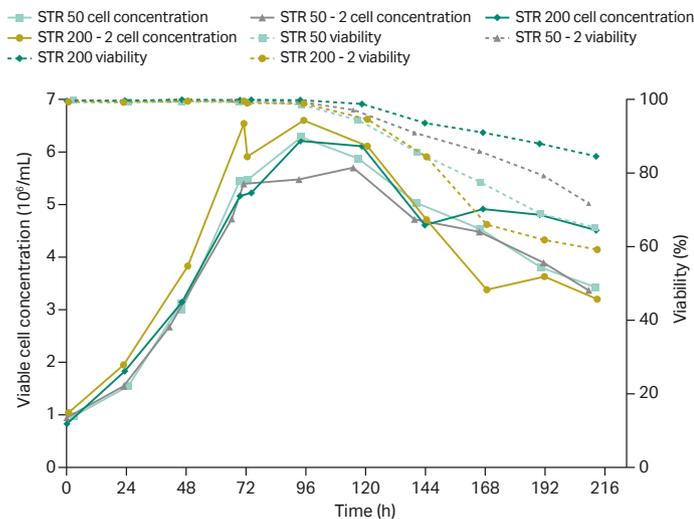
To achieve economically viable production at large scale, standardization is key. Simplified AAV production protocol using ELEVECTA producer cell line reduces handling, which minimizes operator error and time needed for optimization, making the protocol easy to standardize. This standardization facilitates a simple technology transfer to any sister facility or an external manufacturing partner.

## Performance at scale

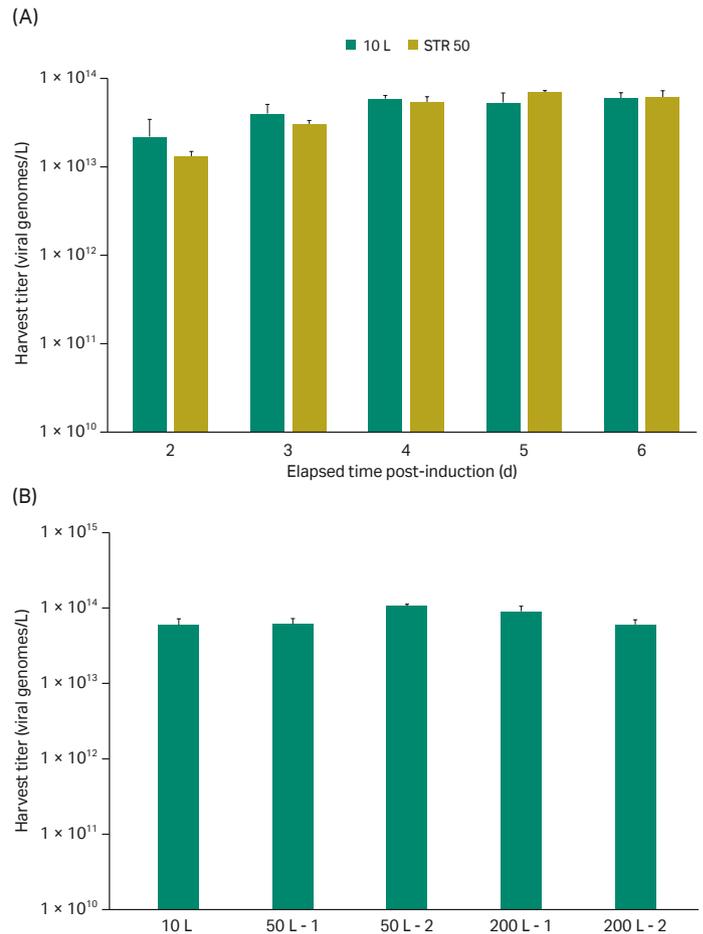
Our proof-of-concept (PoC) producer cell line for AAV8-GFP was successfully scaled up from 10 L to 50 L up to 200 L stirred-tank bioreactors (Fig 2). Consistent cell densities and viabilities of the PoC producer cell line in several 50 L and 200 L bioreactor runs highlight the robustness and scalability of the process. Cells were seeded at  $1 \times 10^6$  cells/mL, and AAV production was started by the addition of induction agent three days post-seeding.

qPCR analysis of viral genome titers (vg/L) from cell suspension samples day 2 to day 6 post-induction show high and consistent productivity throughout scale-up (Fig 3). Batch-to-batch titer consistency was also observed at every scale between the multiple runs.

The scale-up process itself is also straightforward due to the simplified manufacturing process, as the induction step requires no process optimization.



**Fig 2.** Growth and viability profiles for the 50 L and 200 L cultures.



**Fig 3.** Viral genome titer measured by qPCR of the bioreactor cultures after induction of AAV production. (A) 10 and 50 L results for days 2 to 6 post-induction; (B) 10, 50, and 200 L results for day 6 post-induction. Error bars represent standard deviation (assay replicates).

## Regulatory support

Simplicity of AAV manufacturing using ELEVECTA producer cell line is at the heart of the quality by design (QbD) strategy. Production of the AAV particles happens in the same manner for every batch providing a robust manufacturing process as well as consistent product quality, which supports compliance with good manufacturing practices (GMP) regulation and guidelines.

ELEVECTA producer cell line will be transferred to the client with a comprehensive documentation package that Cytiva builds throughout the cell line development project. Cytiva offers extensive quality and regulatory support for documentation relevant for GMP manufacturing as well as regulatory submissions. Our long history in GMP manufacturing means we have in-depth knowledge of hurdles customers frequently face around regulatory submissions. We regularly consult with regulators on different continents to support clients with the foundational knowledge that they can build on when adopting this novel production method of AAV.

# Specifications

Alpha cell line	HEK293 or cell line derived from human amniocytes cells (Cytiva CAP cell line)
AAV serotypes	Common or engineered
Packaging capacity	~ 4.7 kb
Cell banking	Non-GMP research cell bank (RCB)
Upstream process development	Small scale to large scale from FastTrak™ services (optional)
Stability testing	Included

## Ordering information

Please contact your local sales representative or email us as [ELEVECTA@cytiva.com](mailto:ELEVECTA@cytiva.com).

You can also request a quote online at <https://cytiva.link/producer-DF>

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