ENSURING VIRAL VECTOR SUPPLY FOR GENE THERAPIES

Start Right to Scale-Up Right

The potential of gene therapies to cure previously intractable diseases has led to a large number of candidates in the clinic. However, accelerated clinical development schedules can compromise process development

Average Time of Development

REASONS FOR GENE THERAPIES' COMPRESSED DEVELOPMENT TIMELINES

- Urgency to treat and potentially cure diseases with unmet needs
- Encouraging, durable results from early clinical trials
- Pressure to file and launch early

CONSEQUENCES:

- Challenges modifying processes post-registration, as gene therapies are complex, multi-molecular entities
- Difficulties in obtaining enough material, such as viral vectors, for pivotal clinical trials and commercial product
- Labor-intensive and suboptimal processes resulting in high costs

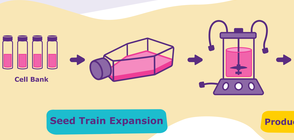
IMPORTANCE OF SCALING METHOD

As clinical development progresses, the quantity of viral vector needed increases. While the adherent cell culture process is used for practical reasons to make early-stage material, it is not ideal for large-scale production. The alternative is to start with a suspension culture, which can be easily scaled-up to meet the demands of pivotal clinical trials and commercial production.

ADHERENT PROCESS – SCALE-OUT

Planar Expansion → **Production Scale**

SUSPENSION PROCESS – SCALE-UP



Seed Train Expansion → **Production Bioreactor (N)**

KEY ADVANTAGES OF A SCALED-UP PROCESS

- Labor-saving, resource-efficient, and more robust than scaling out
- Fewer batches required as each batch can be larger, reducing testing costs
- Better overall process control through increased automation
- Fewer manipulations needed during bioprocessing
- Reduced risk of contamination from the operator and the environment, leading to a safer process overall

KEY CONSIDERATIONS FOR SUCCESSFUL SCALE-UP

PROCESS DESIGN

- Understand your process and the critical parameters required for a consistent high-quality product
- Choose robust analytical techniques for product characterization and lot release
- For upstream processes: use a well-characterized cell line, cost-effective transfection reagent, and chemically defined medium and supplements, all of which should be suitable for cGMP manufacturing of viral vectors
- For downstream processes: select purification products that allow for easy screening activities and easy scale up, with proven quality and supply chain reliability
- For in-process analysis: develop a smart testing strategy to drive process improvement decisions

RAW MATERIALS

- Choose chemically defined media for consistent performance and process reliability
- Use materials suitable for cGMP manufacturing
- Audit your suppliers for supply chain security and production capacity

REGULATORY REQUIREMENTS

- With the added urgency of fast-track approval, ensure that processes at every stage of development are compliant with regulatory requirements

CHALLENGES OF UPSTREAM SCALE-UP

Successful upstream scale-up means adapting cells to suspension culture while maintaining yield and processing larger volumes. But this sometimes results in an unexpected cell density and impurity profile, which can impact downstream processing. Demonstrating product comparability before and after a major process change like this can be challenging for gene therapies because the process can often define what the product is.

MERCK HAS THE SOLUTION TO MAKE YOUR VIRAL VECTOR PROCESS SCALABLE

State-of-the-art upstream production of viral vectors utilizes suspension culture in single-use bioreactors, which enables robust scale-up and productivity.

Merck has developed the VirusExpress™ Lentiviral Production Platform, consisting of a suspension-adapted cell line, a chemically defined medium, and a proven process for the scalable production of lentiviral vectors.

FEATURES AND BENEFITS OF THE VIRUSEXPRESS™ LENTIVIRAL PRODUCTION PLATFORM

- Higher titer and yield than comparable adherent processes
- Clonally-derived cell line and chemically defined medium optimized for virus production
- cGMP manufactured and tested cell banks
- Optimized for transfection with polyethylenimine (PEI)
- Proven performance at clinically relevant scales
- Commercial licensing available

Want to understand how to address the major challenge of scalability in viral vector manufacturing? Check out this webinar on process development for cell and viral gene therapy or learn more about VirusExpress™ platform in this white paper!

Want to work with us?
Reach out to contact@labiotech.eu

Text: Larissa Warneck
Design: Sara Corredor

Created with love at labiotech.eu