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INNOVATOR INSIGHT

Lentiviral vectors: key challenges and new developments

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Gene therapy is no longer an experimental approach. We are now witnessing the advent of genes as medicinal products, based on stable expression of therapeutic genes. Laboratory-borne viruses, also known as viral vectors, can efficiently deliver genes to the cells they infect, with lentiviral vectors (LVVs) one of the most widely used. This article will review existing lentivirus-manufacturing technologies and how they need to be adapted to meet the current market demand, from the perspective of VIVEbiotech – a CDMO manufacturing LVVs to EMA and FDA standards for use in clinical trials.

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THE ADVENT OF NEW CHALLENGES: FROM RESEARCH LAB TO COMMERCIAL PRODUCTION

The regenerative medicine market is growing rapidly. In the first half of 2020, the sector raised $10.7B globally, exceeding the total amount raised in all of 2019. This growing market demands transformative solutions capable of turning a production system designed to provide viral vectors for research, preclinical studies, and small phase I/II clinical trials into fully industrial processes. Many recent reviews describe the key points of the roadmap for manufacturing viral vectors [1,2].

As with any medicinal product, clinical-grade viral vector production must fulfill strict manufacturing, product characterization, and regulatory requirements. However, the unique features of viral vectors are challenging the production capabilities of biotechnology companies. Solutions will only be developed by gathering the expertise of multiple agents, including researchers, clinicians, regulatory experts, specialized CMOs, and CROs, and combining it with the experience gained by the pharmaceutical industry from developing other biological pharmaceutical products [3].

Viral vectors are complex biological products, and innovative approaches will be required to manufacture them at scales that have previously only been reached by long-established biological products, such as monoclonal antibodies or recombinant proteins. Among the different vector types that have reached the clinic, LVVs are the candidate of choice for many indications due to features including permissiveness of the target cell, the ability to accommodate large therapeutic genes, and long-term stable expression in dividing cells.

VIVEbiotech is a European lentivirus-specialized contract development and manufacturing organization (CDMO) that produces vectors for projects from early-stage to GMP manufacturing. At VIVEbiotech, we consider the key aspects for viral-vector manufacturing to be scalability, cost-effectiveness, and wide regulatory compliance. These three aspects need to be carefully addressed to adequately meet the increasing market demands [4]. While it is important to note that certain intrinsic characteristics of lentiviruses make small- and large-scale production challenging, this article will focus on the key aspects that impact on lentivirus manufacture and analyze their importance in scaling up cGMP-grade LVV production, with special emphasis on those features that VIVEbiotech is working on.

LENTIVIRUSES ARE MORE THAN SIMPLE GENOMES COVERED BY PROTEINS: FEATURES TO CONSIDER FOR INDUSTRIAL PROCESSES

LVVs are enveloped viruses, which means they are fully mature and functional upon budding from the cell. From the manufacturing point of view, this represents a challenge, as the extracellular bioproduct needs to retain this highly ordered architecture in addition to at least two enzymatic activities: the integrase and the retrotranscriptase. Upstream (USP) and downstream (DSP) processing must be carefully performed to preserve these biological activities. The sensitivity of such bioproducts to environmental conditions [5] impacts manipulation, handling, and storage throughout the production chain.

From the bioengineering point of view, production of LVVs is a continuous cellular process shedding viral vectors to the culture media in a process that lasts only a few days. This differs from the bulk production of infectious viruses or vaccines, which can be harvested within much wider time windows.

Viral stability in static (tissue culture flask) settings is higher than in dynamic (bioreactor) settings, and we at VIVEbiotech have found in internal studies that this is one of the most critical aspects impacting the biological activity of manufactured batches. Large multilayer systems like Cell Factory™ (Thermo Fisher Scientific) or HYPERStack® (Corning) are the most commonly used plasticware to produce LVVs for the clinic. However, these

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systems are not scalable to market needs [3], and further development is required to obtain the desired yields in these bioreactors.

Thus, the transition towards an industrial process cannot simply be done by transferring know-how and well-established low-scale manufacturing procedures, nor by extrapolating the pharmaceutical production processes of monoclonal antibodies or recombinant proteins [6,7].

PRODUCTIVITY CHALLENGES: NEEDS AND SOLUTIONS

The key goals for companies producing LVVs are:

- **Titers:** Generating sufficiently large quantities of functional LVVs, necessary to obtain high titers.
- **Purity:** Optimizing DSP to obtain purer LVVs.
- **Functionality:** Ensuring highly functional LVVs to achieve the required target-cell–transduction levels.

Titers

Net production is the ratio between the number of functional vectors produced per packaging cell and the stability of the extracellular biological product. This is a multifactorial parameter in which physical conditions, chemical composition, and biological interactions between vectors, cells, and by-products have an impact. VIVEbiotech is currently working on the enhancement of net production, as there is great scope for increasing the titers that global CDMOs are reaching.

It has been shown by several groups that, when using classical LVV manufacturing approaches, between 70–90% of viable particles are lost by the transduction of producer cells, in a process called retro-transduction [8,9]. To address this problem [10], VIVEbiotech's R&D Department is developing a cell line that does not permit retro-transduction and would therefore give higher titers.

Purity

Purification of LVVs is an extremely sensitive procedure due to the aforementioned properties of the virions. The majority of current DSP techniques rely on separating vector particles based on their physical characteristics. Anion-exchange chromatography, filtration (depth filtration, tangential flow filtration [TFF]), and sterile filtration are performed at different phases of the manufacturing process to purify and concentrate the vector, and to reduce the generated contaminants [11,12].

The two steps that present the greatest challenges during vector purification are capture and sterile filtration. Anion-exchange chromatography – either resin-, membrane-, monolith-, or affinity-based – has been greatly improved for LVV purification, but recovery of the product remains a bottleneck [2]. Although recovery after TFF can be high (>97%), the overall LVV recovery is usually around 30% [13].

VIVEbiotech has increased its average DSP recovery by more than a 50% in comparison with the average percentages shown in prior publications by other groups by applying key improvements, particularly during endonuclease treatment and anion-exchange chromatography (unpublished data).

LVV recovery performances are highly relevant, as the purity of the LVV-based final product has been demonstrated to have a great impact on the transduction efficiency of the target cells. Given that the use of LVVs for in vivo approaches is becoming more frequent, the optimization of USP and DSP is even more critical [14].

Until now, the affinity purification of VSV-pseudotyped LVVs has been affordable by the use of specificity methods based on heparin or derivatives [15]. However, alternative methods have recently been developed by the addition of tags to the protein structure that aid in specific affinity purification

[16]. We consider it a high priority to analyze in-depth the composition of the envelope of the LVVs, as it will be crucial for the development of other affinity adsorption methods in the future [15]. This is an additional research line which VIVEbiotech is currently working on.

Functionality

The required virion needs are determined by the therapeutic indication. The batch size is dependent on:

- The target cell/tissue
- The number of cells that need to be transduced to achieve the desired therapeutic effect, and
- The efficiency with which the LVVs transduce these target cells.

Efficiently transducing the target cell is in most cases the last hurdle to overcome, as this requires shaping the biology of the vector to infect a cell very reluctant to be infected. Human hemopoietic stem cells and T cells express few receptors for VSVg, the most commonly used lentiviral vector pseudotype, and from a virological point of view should be considered resistant to transduction/infection. Thus, prior activation of those cells is required before transduction, an issue that must be balanced with stemness and functional maintenance.

Any improvements in transduction rates will increase the number of patients that can be treated by a batch, ultimately making these therapies more affordable and cost-effective. The use of transduction enhancers is a promising strategy aimed at diminishing the vector multiplicity of infection (MOI). LentiBOOSTTM (SIRION Biotech, www.sirion-biotech.com) and Vectofusin®-1 (Milteny-Biotech, www.miltenyibiotec.com) have demonstrated the ability to reduce the virus needs by 20-fold, depending on the cell type [17].

As the permissivity to lentivirus transduction of target cells not only relies on the receptors but also on the viruses themselves, pseudotyping can be the strategy of choice to transduce certain cell types more efficiently. Highly relevant studies have demonstrated the great impact that a different pseudotyping approach can have on the final functionality of target cells [18–20]. For this reason, pseudotyping is, and will continue to be, one of the major vector characteristics to be considered on the road to improving LVVs.

It is well known that the final physical configuration of a vector impacts its properties and that these properties have an effect on net production [20–22]. It is important not only to work on pseudotyping strategies that can enhance transduction but on the optimization of the production process itself, while bearing in mind the regulatory requirements these advanced therapy products must comply with [23].

VIVEBIOTECH'S APPROACH

VIVEbiotech has manufactured more than 100 batches since its creation in 2015, and will soon increase its capabilities to allow for the manufacturing of more than 80 GMP-grade batches per year. The company will continue to use fixed-bed bioreactors (FBR) for adherent cells in the short term and consider implementing new technologies, such as suspension-based manufacturing using stirred tank reactors (STR), in the mid-term.

We at VIVEbiotech are using both Pall Corporation and Univercells reactors; the former for small-scale production, and the latter for a wide range of scales. The great variability of bioreactors we use allows manufacturing from developmental- to commercial-scale batches, providing large surface areas – from 2.4 to 600 sqm- for culturing adherent cells, and permits tight regulation of several production parameters, enabling optimized cell growth and productivity [24].

VIVEbiotech and others have evaluated the potential of FBRs and have detected

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some critical aspects that need to be improved. Specifically, compared to non-adherent STRs, certain issues need further improvement in adherent cell systems, such as (i) larger scales, (ii) simpler online parameter measurement, and (iii) cell distribution homogeneity along the height of the fixed bed. Many of these points have recently been approached by our Director of Operations in a recent article [24].

STABLE PRODUCER CELL LINES: THE FUTURE OF LVV PRODUCTION?

The majority of past and present LVV-producing methodologies are based on overexpressing plasmid DNA in the highly transfectable human HEK293 cell line. The fact that the production process is so dependent on transfection brings severe drawbacks for industrializing an LVV manufacturing process [25–28]. The elimination of this transfection step would result in higher cost-effectiveness and reproducibility. This is why stable producer cells have been developed; however, defects due to toxicity, counterselection of cells, chromosomal silencing, and relatively low yields [29–31] must be considered as factors negatively affecting their use for GMP manufacturing. To our knowledge, none of these stable packaging cell lines have been used for manufacturing clinical-grade LVVs.

VIVEbiotech is addressing the producer cell line issue using a novel approach. We are developing a producer system based on expression of the helper functions, led by a non-integrative lentiviral vector named LentiSoma. VIVEbiotech has secured worldwide rights to this patented product, which allows long-term maintenance of circular stable DNA that does not integrate into the chromosomes but remains stable through cell division, with undetectable loss of expression – a feature not shared by any existing LVVs.

Using this LentiSoma vector, a stable producer cell line called VIVESOMA is being built that has the potential to overcome some of the drawbacks observed in other producer lines due to integration issues like loss of integrated copies, silencing, high clonal variability due to integration of variable copy numbers, etc. LentiSoma produces levels of helper proteins based on a known, low number of episomal copies devoid of lentiviral sequences (Figure 1). The design is supplemented with a last-generation on/off system to silence the expression of the helper genes very precisely, allowing production in the absence of drugs, and limiting the toxicity of the intermediate products that severely affect cell viability.

In parallel, VIVEbiotech is optimizing its transient transfection process and has reduced the number of plasmids required (both transfer and helper) significantly. (Figure 2). This is having a great impact in reducing both associated plasmid costs and DNA impurities in the final product.

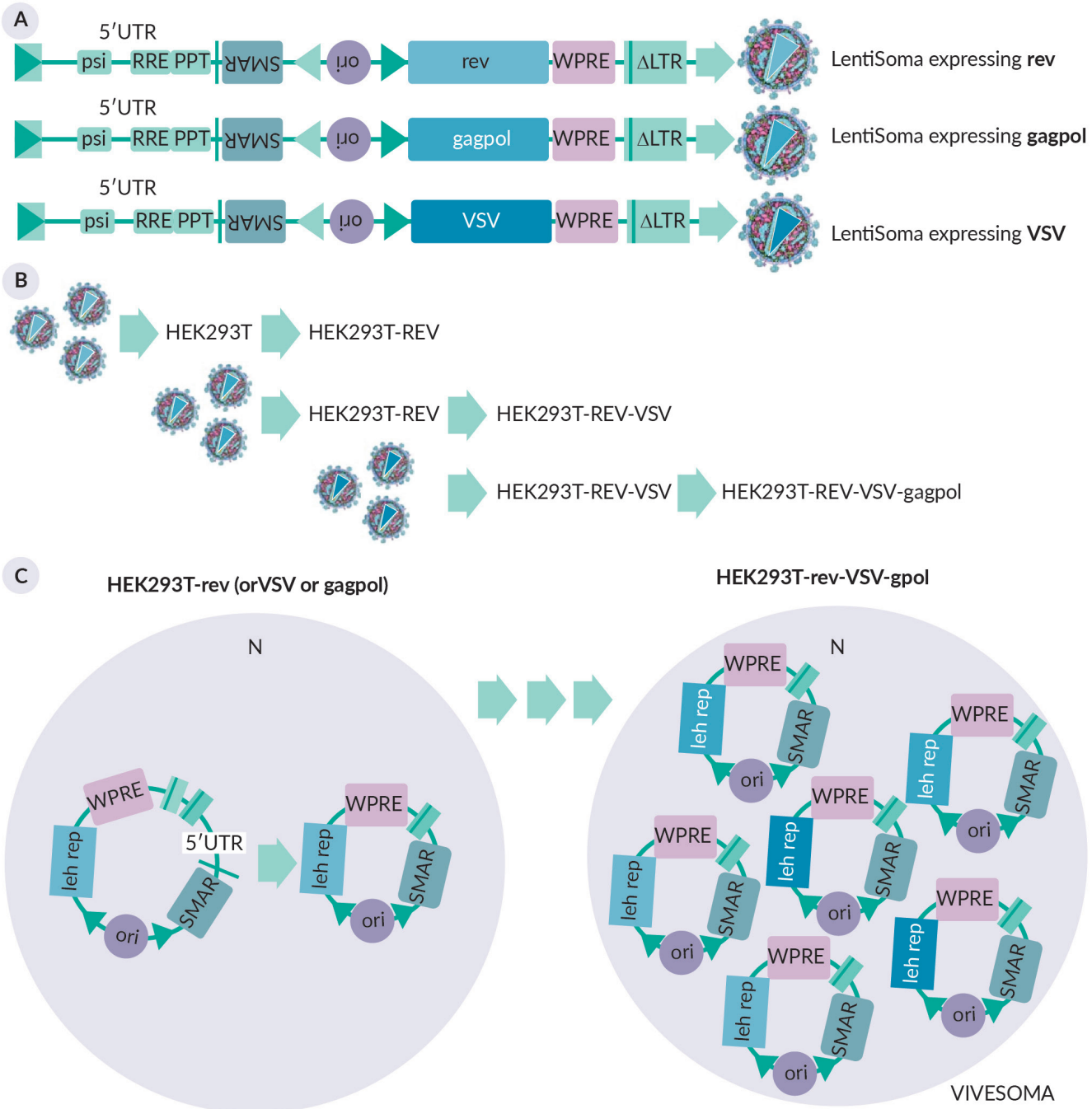
DEEPER ANALYSIS OF FINAL PRODUCT TO ASSESS FUNCTIONALITY

Medicinal products intended for use in humans must be very carefully characterized. Manufacturers must address a large number of contaminants that challenge regulatory requirements due to their impact on biosafety. To our knowledge, the exact contents of the intermediate and final product consisting of a lentivirus have only been described once in the published literature [32]. The existing cellular and subcellular byproducts present in the final formulation have a considerable impact on toxicity and biological activity, and thus on the required dosing to transduce enough target cells.

Purification techniques are evolving rapidly, which will assist manufacturers in obtaining LVVs of a significantly higher quality. VIVEbiotech is performing a systematic study aimed at elucidating the effect of several USP and DSP steps, and some other specific physicochemical modifications of virion composition, by high-performance lipidomic technologies.

FIGURE 1

Stable producer cell line VIVESOMA.



(A) Genetic structure of the elements contained in every transfer plasmid aimed at generating LentiSoma-expressing helper genes (rev, VSV, and gagpol) represented in blue. **(B)** Schematic representation of the steps followed to sequentially generate a HEK293T cell expressing the helper genes by LentiSoma. **(C)** The cartoon depicts the stable circular DNA generated upon transduction with every LentiSoma, and the final minimal structure stabilized with almost no lentiviral-derived sequences.

VIVEbiotech is also developing a program in which components within the cGMP-grade LVV batches are being characterized for the first time by state-of-the-art 2D-cryo-electron microscopy (CEM) and 3D-cryo-electronic-tomography (CET) techniques. These techniques will allow for analysis of the morphology, integrity, size distribution, purity, and aggregation by transmission electron microscopy (TEM).

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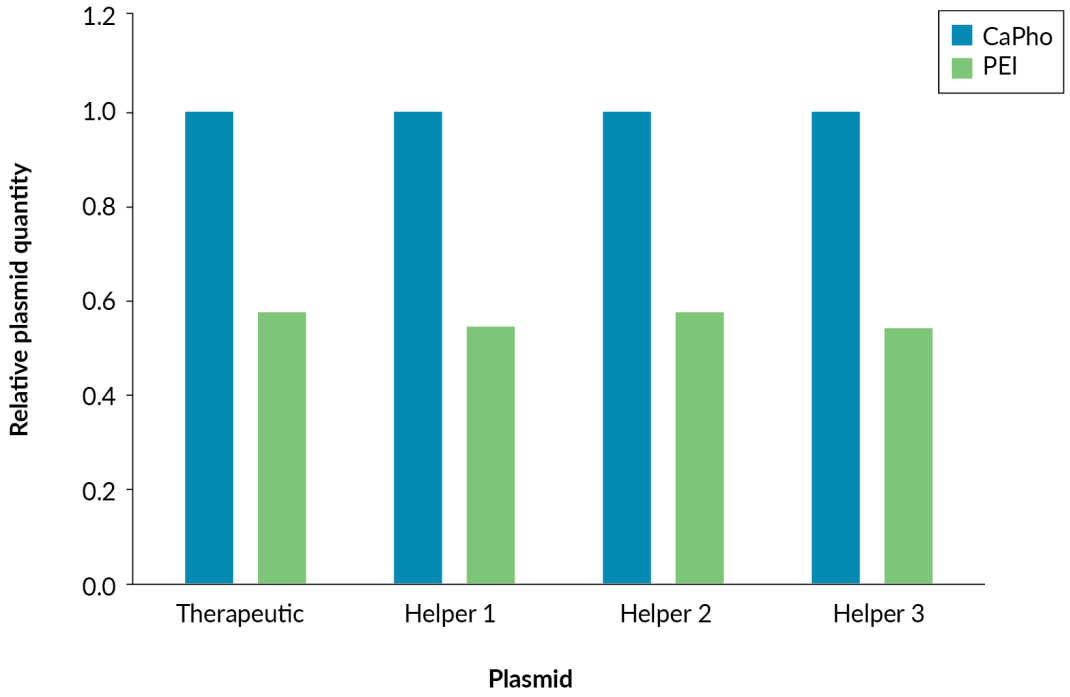
FIGURE 2

The use of PEI instead of calcium-phosphate (CaPho) allows a reduction in more than half the mass of every plasmid to reach similar yields in LVV production under identical transfection efficiencies.



Preliminary examination has shown that within VIVEbiotech´s batches, morphogenically fully mature particles are present together with a panoply of vesicles of several sizes and features, as well as a collection of LVV-derived particles. VIVEbiotech, in collaboration with CICbioGUNE, is defining, quantifying, and characterizing these particles co-purified with the LVVs [33]. TEM and lipidomic technologies will enable not just the design of a more specific purification process but will also enable deep characterization of the biological activity of some of these particles.

ANALYTICS

The need to urgently implement more precise control systems, mainly in USP phases, has recently become a topic of discussion within the industry [34,35]. Biomanufacturers are shifting from "Quality by Testing" where product quality is assessed at the end of the process, to "Quality by Control," where product quality is monitored and adjusted during the process [36].

Large-scale manufacturing cannot be solely dependent on the values obtained by sensors monitoring pH, metabolites, pressures of gases, and permittivity. We need multidisciplinary groups composed of physicochemists, engineers, mathematicians, and biologists to come together and develop novel technologies based on microfluidics, optical, electrical, and electrochemical detection techniques, micro-immunoassays, micro PCR, novel biomaterials, Raman spectroscopy, single-cell analysis, 2D fluorescence, near-infrared spectroscopy, RNA-omics, and more, in order to generate comprehensive quality assessments. This should be complemented with the use of bioinformatics, biostatistics, and data management, assisted by depth data analysts and the latest generation software. Together, these advanced analytics will help move the field towards BioProcessing 4.0 [37].

Additionally, the pharmaceutical industry recognizes the need for a well-characterized reference standard that will allow comparison of results from different laboratories and CDMOs. This would permit the establishment of appropriate clinical dosing [38] and would enable the setting of titers on reference cell lines in order to objectively compare LVVs manufactured in any facility. Initiatives like the "Lentivirus Vector Reference Standard Initiative - ISBioTech [39] are greatly needed to solve this issue. VIVEbiotech, as one of the CDMOs in the field, hopes to be one of the actors involved in defining the reference standard.

CONCLUDING REMARKS

Gene therapy is now a clinical reality and has the potential to treat or cure diseases of varied origins, from rare diseases to cancer. Due to the effectiveness of these therapies, and the high number of patients that can benefit from them, the market is growing exponentially. The journey toward commercialization is not yet well established, leaving each developer to forge their own path [40,41]. Focusing on the industrialization of production processes, while achieving cost-effectiveness and wide regulatory compliance, is key.

REFERENCES

1. Ansorge S, Burnham M, Kelly M, Jones P. Scale-up considerations for improved yield in upstream viral vector production. *Cell Gene Therapy Insights* 2019; 5(12): 1719–1725.
2. McCarron A, Donnelley M, McIntyre C, Parsons D. Challenges of up-scaling lentivirus production and processing. *J. Biotechnol.* 2016; 240: 23–30.
3. Ensuring viral vector and gene therapy commercial readiness. *Cell Gene Therapy Insights* 2020; 6(2): 85–92.
4. Masri F, Cheeseman E, Ansorge S. Viral vector manufacturing: how to address current and future demands? *Cell Gene Therapy Insights* 2019; 5(Suppl. 5): 949–970.
5. Carmo M, Alves A, Rodrigues AF, Coroadinha AS, Carrondo MJT, Alves PM, Cruz PE Stabilization of gammaretroviral and lentiviral vectors: from production to gene transfer. J Gene Med. 2009; 11: 670–678.
6. McCarron A, Donnelley M, Parsons D. Scale-up of lentiviral vectors for gene therapy: advances and challenges. *Cell Gene Therapy Insights* 2017; 3(9), 719–729.
7. Lesch HP. Back to the future: where are we taking lentiviral vector manufacturing? *Cell Gene Therapy Insights*.
8. Pan Y-W, Scarlett JM, Luoh TT, Kurre P. Prolonged adherence of human immunodeficiency virus-derived vector particles to hematopoietic target cells leads to secondary transduction in vitro and *in vivo*. *J. Virol.* 2007; 81(2): 639–649.
9. Ohishi M, Shioda T, Sakuragi JI. Retro-transduction by virus pseudotyped with glycoprotein of vesicular stomatitis virus. *Virology* 2007; 362: 131–138.
10. May M. Gene therapy dollar is waiting on viral vector dime. Genetic Engineering and Biotechnology News 2020 Feb 1. Available at: www.genengnews.com/topics/bioprocessing/gene-therapy-dollar-is-waiting-on-viral-vector-dime/
11. Bandeira V, Peixoto C, Rodrigues AF *et al.* Downstream processing of lentiviral vectors: releasing bottlenecks. *Hum. Gene Ther. Methods* 2012; 23(4): 255–263
12. Moss D. Vector purification: issues and challenges with currently available technologies. *Cell Gene Therapy Insights* 2019; 5(9): 1125–1132.
13. Cooper AR, P Sanjeet, Senadheera S, Plath K, Kohn DB, Hollis RP. Highly efficient large-scale lentiviral vector concentration by tandem tangential flow filtration. *J. Virol. Methods* 2011; 177: 1–9.
14. Emek B. Addressing challenges presented for downstream purification by changes upstream. *Cell Gene Therapy Insights* 2019; 5(Suppl. 2): 197–201.
15. Segura MM, Kamen A, Garnier A. Downstream processing of oncoretroviral and lentiviral gene therapy vectors. *Biotechnol. Adv.* 2006; 24(3): 321–337.
16. Münch RC, Mühlebach MD, Schaser T *et al.* DARPins: An efficient targeting domain for lentiviral vectors. *Mol. Ther.* 2011; 19(4): 686–693.
17. Piovan C, Marin V, Scavullo C *et al.* Vectofusin-1 promotes RD114-TR-pseudotyped lentiviral vector transduction of human HSPCs and T lymphocytes. *Mol. Ther. Methods Clin. Dev.* 2017; 5: 22–30.

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18. Bell AJ Jr, Fegen D, Ward M, Bank A. RD114 envelope proteins provide an effective and versatile approach to pseudotype lentiviral vectors. *Exp. Biol. Med.* 2010; 235: 1269–1276.

19. Van-den-Driessche T, Chuah MK. Targeting endothelial cells by gene therapy. *Blood* 2013; 122: 1993–1994.

20. Girard-Gagnepain A, Amirache F, Costa C *et al.* Baboon envelope pseudotyped LVs outperform VSV-G-LVs for gene transfer into early-cytokine-stimulated and resting HSCs. *Blood* 2014; 124(8): 1221–1231.

21. Frecha C, L.vy C, Cosset F-L, Verhoeyen E. Advances in the field of lentivector based transduction of T and B lymphocytes for gene therapy. *Mol. Ther.* 2010; 18: 1748–1757.

22. Levy C, Amirache F, Girard-Gagnepain A *et al.* Measles virus envelope pseudotyped lentiviral vectors transduce quiescent human HSCs at an efficiency without precedent. *Blood* Advances 2017; 1: 2088–2104.

23. Joglekar A, Sandoval S. Pseudotyped Lentiviral Vectors: One Vector, Many Guises. *Hum. Gene Ther. Methods* 2017; 28(6): 291–301.

24. Mirasol F. Modernizing bioprocessing for gene therapy viral vectors. Pharmaceutical Technology 2020; 44(10): 28–33. Available at: www.pharmtech.com/view/modernizing-bioprocessing-for-gene-therapy-viral-vectors

25. Ansorge S, Lanthier S, Transfiguracion J, Durocher Y, Henry O, Kamen A. Development of a scalable process for high-yield lentiviral vector production by transient transfection of HEK293 suspension cultures. *J. Gene Med.* 2009;11(10): 868–876.

26. Tomás HA, Rodrigues AF, Carrondo MJT *et al.* LentiPro26: novel stable cell lines for constitutive lentiviral vector production. *Sci. Rep.* 2018; 8: 5271.

27. Sanber K, Knight S, Stephen S *et al.* Construction of stable packaging cell lines for clinical lentiviral vector production. *Sci. Rep.* 2015; 5: 9021.

28. A Stornaiuolo, B M Piovani, S Bossi *et al.* RD2-MolPack-Chim3, a packaging cell line for stable production of lentiviral vectors for anti-HIV gene therapy. *Hum. Gene Ther. Methods* 2013; 24: 228–240.

29. Gama-Norton L, Herrmann S, Schucht R *et al.* Retroviral Vector Performance in Defined Chromosomal Loci of Modular Packaging Cell Lines. *Hum. Gene Ther.* 2010; 21(8): 979–991.

30. Ikeda Y, Takeuchi Y, Martin F, Cosset FL, Mitrophanous K, Collins M. Continuous high-titer HIV-1 vector production. *Nat. Biotechnol.* 2003; 21(5): 569–572.

31. Kinsella TM, Nolan GP. Episomal vectors rapidly and stably produce high-titer recombinant retrovirus. *Hum. Gene Ther.* 1996; 7(12): 1405–1413.

32. Richieri SP, Bartholomew R, Aloia RC *et al.* Characterization of highly purified, inactivated HIV-l particles isolated by anion exchange chromatography. *Vaccine* 1998; 16(2–3):119–129.

33. Böker K, Lemus-Diaz N, Ferreira R, Schiller L, Schneider S, Gruber J. The impact of the CD9 tetraspanin on lentivirus infectivity and exosome secretion. *Mol. Ther.* 2018; 26(2): 634–647.

34. Moscariello J. Preparing an *ex vivo* gene therapy process for process validation. *Cell Gene Therapy Insights* 2019; 5(4): 517–522.

35. Burnham M. Building a LVV characterization and process validation strategy. *Cell Gene Therapy Insights* 2019; 5(4): 511–515.

36. Lipsitz Y, Timmins NE, Zandstra PW. Quality cell therapy manufacturing by design. *Nat. Biotechnol.* 2016; 34, (4): 393.

37. May M. Debottlenecking opportunities clearer with a bioprocessing 4.0 perspective. Genetic Engineering and Biotechnology News. 2020 Jul 6; 40(7). Available at: https://www.genengnews.com/insights/debottlenecking-opportunities-clearer-with-a-bioprocessing-4–0-perspective/

38. Lesch HP. Back to the future: where are we taking lentiviral vector manufacturing? *Cell Gene Therapy Insights* 2018; 4(11): 1137–1150.

39. Zhao Y, Stepto H, Schneider CK. Development of the first World Health Organization Lentiviral Vector Standard: toward the production control and standardization of lentivirus-based gene therapy products. *Hum. Gene Ther. Methods* 2017; 28(4): 205–214.

40. Meagher M, Krishnan M, Davies C. Uncharted Territory: Top challenges facing gene therapy development. Genetic Engineering and Biotechnology News. 2021 Jan 8; 41(1). Available at: https://www.genengnews.com/roundup/uncharted-territory-top-challenges-facing-gene-therapy-development-2/

41. Pedro F. Costa. Translating bio-fabrication to the Market. *Trends Biotechnol.* 2019; 37(10): 1032.

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