Process Chromatography

Got Purification Troubles?
Efficient Downstream Purification of Viral Vectors

The Challenge

Need to purify antigen proteins rapidly at massive scales? Lentiviral vectors (LVVs) show great therapeutic promise. However, their purification at large scale while maintaining stability to achieve high recovery of infectious LVVs and good clearance of host cell proteins (HCPs) can be challenging. Since affinity-based protein purification can limit antigen yields, high-throughput screening of nonaffinity methods can provide a roadmap for developing population-scale purification processes for tens of millions of vaccine doses per day.

Purification Tip

Ghosh et al. (2022) highlight the importance of identifying and using mobile phase conditions that maintain LVV stability during the purification process. Specifically, the authors found that phosphate buffers in the pH range of 6.5–7.5 with low to moderate salt concentrations provided good stability for LVVs.

Additionally, the study demonstrated the potential of weak anion exchanger resins to achieve high levels of HCP clearance in the flowthrough or low-salt wash, followed by elution of LVVs at moderate salt concentrations, enabling the development of efficient bind and elute processes.

Authors' Approach

Ghosh et al. (2022) systematically evaluated LVV stability and developed an optimized ion exchange purification process using Macro-Prep™ High Q Resin with the following results.

- High-throughput screening identified Macro-Prep High Q Resin as providing >50% LVV recovery
- The optimized step-gradient achieved 78% LVV recovery by RT-qPCR with 82% infectivity
- The process resulted in >2.5 log clearance of host cell protein
- Macro-Prep High Q outperformed three other resins tested for protein clearance

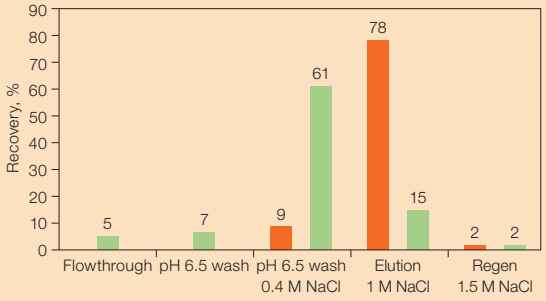

Fig. 1. LVV elution recovery and protein clearance for step elution with Macro-Prep High Q Resin. Chromatography steps shown with LVV titer (■) and protein amount (■) measured in duplicates using RT-qPCR and Bradford assay, respectively. The pool volume in all fractions is 10 CV. Regen, resin regeneration.

Table 1. Results of the optimized step elution process indicating LVV recovery and HCP clearance achieved with Macro-Prep High Q Resin. LVV recovery was measured using orthogonal techniques: total viral RNA by RT-qPCR, capsid p24 protein content by p24 enzyme-linked immunosorbent assay (ELISA), and infectivity by a transduction assay. An ELISA for residual HCP (HEK 293) was also performed.

	LVV Recovery, %			HCP Clearance, LRV
Resin	RT-qPCR	p24 ELISA	Infectivity	HEK 293 HCP ELISA
Macro-Prep High Q	78	86	82	2.51

HCP, host cell protein; HEK, human embryonic kidney; LRV, logarithmic removal value; LVV, lentiviral vector; RT-qPCR, reverse transcription quantitative PCR.

Visit bio-rad.com/Macro-PrepHighQ for more information.

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Macro-Prep High Q strong anion exchange resin contains quaternary amine functional groups and is ideal for purifying acidic and neutral proteins and peptides.

Properties of Macro-Prep High Q Resin include:

- Large 50 µm particles provide high flow rates and easy scale-up
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- Excellent chemical stability and compatibility with common buffers
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Reference

Ghosh R et al. (2022). Evaluation of lentiviral vector stability and development of ion exchange purification processes. Biotechnol Prog 38, e3286.

Note: This flyer is based on the study conducted by Ghosh et al. (2022) and is intended for information purposes only. It is recommended to consult the original study and perform additional validation experiments according to specific requirements.

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