Scalable lentiviral vector production using stable producer cell lines in perfusion mode

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Scalable Lentiviral Vector Production Using Stable Producer Cell Lines in Perfusion Mode

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Lentiviral vectors (LV) are used for gene and cell therapy

- HIV-based, enveloped virus
- Fragile, sensitive to pH and temperature
- Stable gene integration into genome of dividing and non-dividing cells

→ Gene therapy, CAR-T
Bioprocessing of Lentiviral vectors (LV)

- Currently, LV are mainly produced in adherent cells by transfection of 4 plasmids: Virus accessory genes (Gag/Pol, Rev and VSV-G) and the gene of interest.

Objective: PD for stable producer cell lines (production of LV under the control of two switches) in suspension.
LV titers obtained under different modes of operation

- **Total Yield with different modes of operation**

<table>
<thead>
<tr>
<th>Mode of Operation</th>
<th>Total yield (TU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Batch (n=7)</td>
<td>2.09E+10</td>
</tr>
<tr>
<td>Fed-batch (n=2)</td>
<td>3.54E+10</td>
</tr>
<tr>
<td>Perfusion (n=4)</td>
<td>1.91E+11</td>
</tr>
</tbody>
</table>

10-fold yield increase when operating in perfusion mode (sequential harvests): Manceur et al, Human gene Therapy, 2017

**Perfusion: Comparison of different cell retention systems**

- **Perfusion with an acoustic filter**
  - Functional titer (TU/ml) vs Time (dpi)
  - No sequential harvesting with ATF

- **Perfusion with an ATF filter (0.5µm - PES)**
  - 2 log decrease

→ No sequential harvesting with ATF
LV production and purification: towards ‘continuous’ bioprocessing

1. Transfer to GMP
2. Cost analysis/optimization/LV stability
3. Integrate USP and DSP
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