Smart polymers targeting VSV-G accurately **detect lentivirus** in **Octet® BLI** platform and show promise for novel capture chromatography

Novel synthetic affinity reagents for lentivirus analytics and capture chromatography

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Introduction

Synthetic affinity reagents targeting VSV-G, a lentivirus envelope protein, have been designed to increase the performance of lentiviral based processes in analytics and purification. Smart polymer analytical performance has been demonstrated on the Octet® biolayer interferometry (BLI) platform. A bind-and-release mechanism has been demonstrated in a prototype purification set-up, indicating the possibility to go beyond analytics and vastly improve lentivirus yields during downstream processing.

Methodology

In silico modelling was used to assess the surface of VSV-G envelope protein (Figure 1) and to screen a monomer library (the building blocks of smart polymers). Multiple compositions were identified, which were then synthesized using solid phase imprinting and screened using surface plasmon resonance (SPR) to identify leading candidates (Figure 2). Leading candidates were then immobilized onto ARG2 biosensors, integrated into the Octet® BLI device, and screened against multiple batches of lentivirus. To demonstrate a purification concept, VSV-G smart polymers were immobilized on a membrane and a lentivirus surrogate (gold-conjugates of VSV-G) was captured and released under mild conditions.

Results

A response was shown on the Octet BLI instrument (Figure 3), consistent across multiple lentivirus batches of titers in the range of 1 x 10^5 to 1 x 10^7 TU/mL. The purification prototype visually demonstrated the bind and release of the lentivirus surrogate under mild conditions (Figure 4).

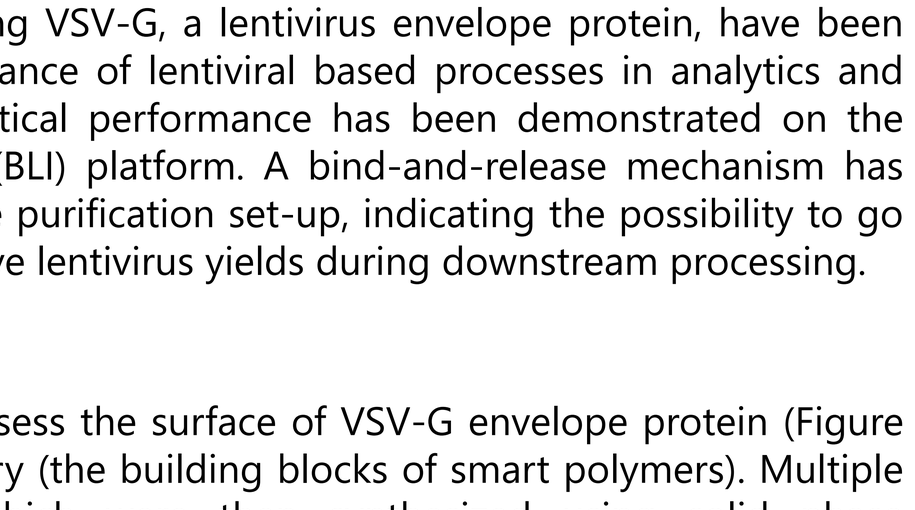


Figure 3. BLI response showing specific binding of Nuclight Lentivirus to the leading VSV-G smart polymer.

Figures

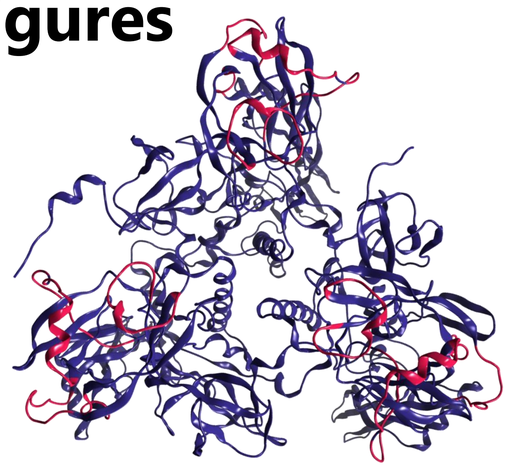
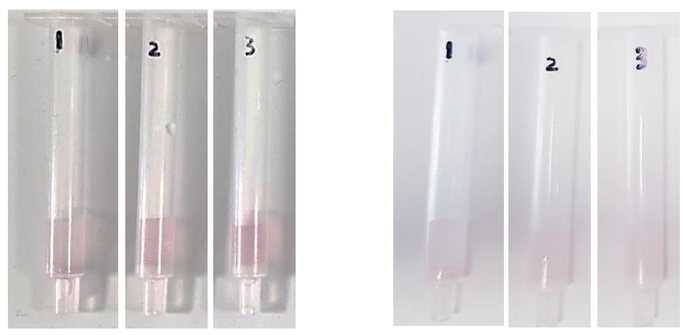


Figure 1. ***In silico*** molecular modelling of VSV-G protein to identify target surface epitopes (red regions) for smart polymer development.

Surface Epitopes	No. Compositions Produced	No. Leading candidates via SPR	No. Leading candidates via BLI
1	9	6	2
2	10	7	1
3	7	1	
4	4	4	
5	7	1	
6	7		
7	6		

Figure 2. Diagram of the composition selection process to select leading smart polymer candidates.



Bound surrogate lentiviral particles

Post surrogate particle release

Figure 4. Bind-and-release mechanism utilising lentivirus surrogate particles under mild release conditions.

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