Enabling improved bioprocessing solutions with Optimer®

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Introduction

- Current protein-based affinity ligands are unable to resolve a range of complex protein purification problems resulting in:
  - impurity challenges
  - multi-step chromatography processes
  - target limitations
  - limited yields
  - poor cost-efficiencies
- Optimer ligands are next generation aptamers with a broader target range to enable new therapeutic modalities and the ability to select ligands with controlled capture and release characteristics for improved yields and cost-of-goods.
- A number of commercial case studies are presented where Optimer ligands are enabling solutions to these bioprocessing challenges for our partners.

Case study 1: Improving the yield of fragile therapeutic protein targets with Optimer

- Our partner's existing purification process required harsh elution conditions resulting in 80% of the product being lost during purification.
- Optimer ligands were developed that bind to the therapeutic protein under customer-specified conditions and release the protein under gentle elution conditions (fig.1 & 2) to maintain the functionality of the biologic and increase the process yield.

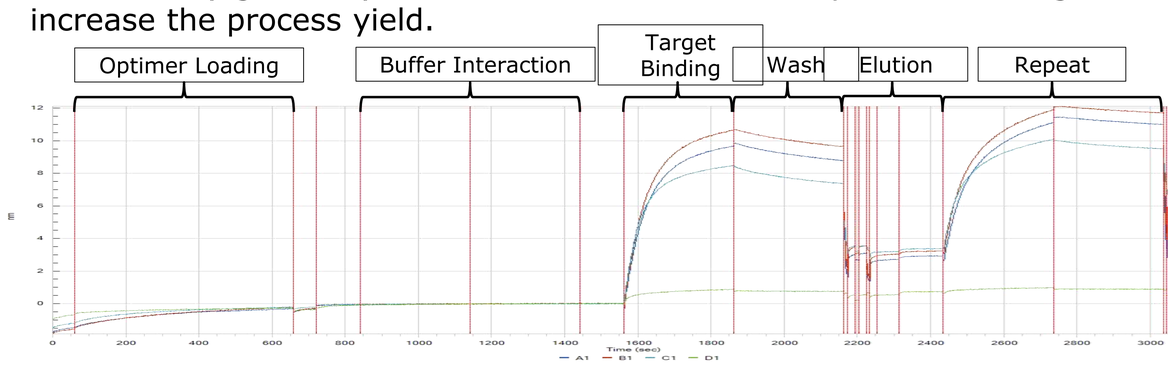

Figure 1: Biolayer interferometry (BLI) shows the developed Optimer ligand binds and releases the target therapeutic protein across multiple cycles under the required gentle elution conditions.

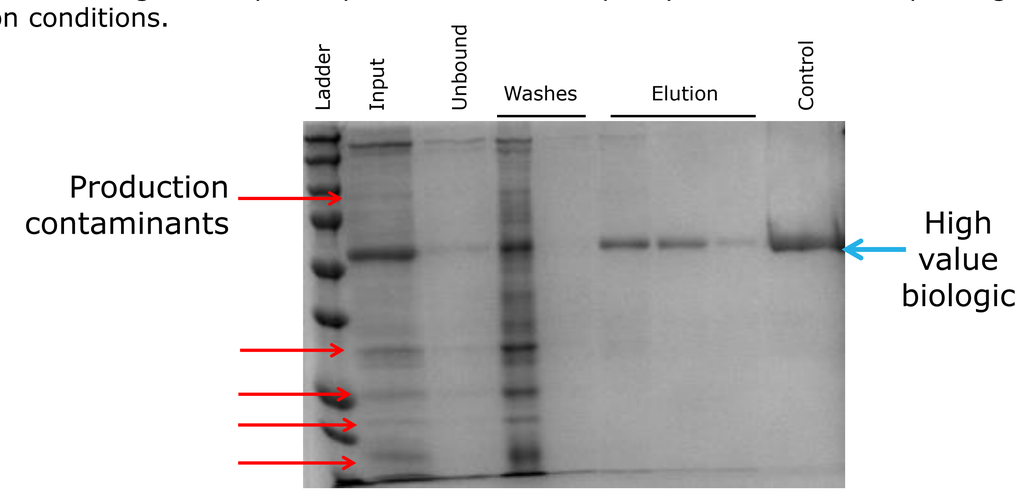

Figure 2: Optimer-functionalisation of small scale columns show a high level of purification of the target therapeutic protein in a single pass via SDS-PAGE.

Case study 2: Using Optimer to purify a multi-subunit protein complex

- Purification of a multi-subunit protein was required to support vaccine development.
- Optimer ligands were developed that bind to the protein complex when present in the partners feedstock and elute all complex constituents under gentle conditions sufficient to protect the target (fig. 3 & 4).

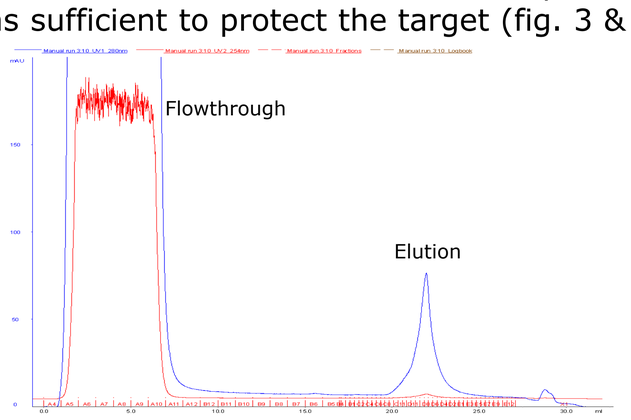

Figure 3: Small scale purification was demonstrated using an Optimer-functionalised column on an AKTA Explorer FPLC system.

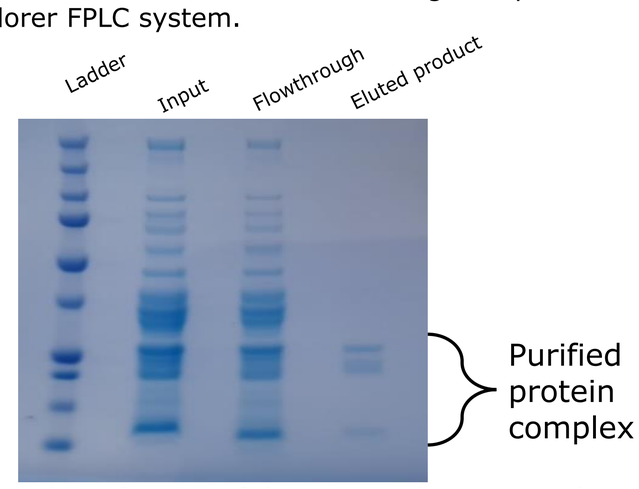

Figure 4: SDS-PAGE showed purification of the expected protein and retention of each of the protein subunits by the Optimer purification ligand.

Case study 3: Using Optimer to improve purified biologic quality

- A commercial affinity purification process for a therapeutic protein consistently co-purified a contaminant with the target molecule.
- Optimer ligands were developed that bound to the therapeutic protein present in their feedstock and were able to elute under gentle conditions sufficient to protect the therapeutic (fig 5 & 7).
- Negative selection was incorporated into Optimer discovery to ensure the ligands did not bind to the co-purified contaminant (fig. 6 & 8).

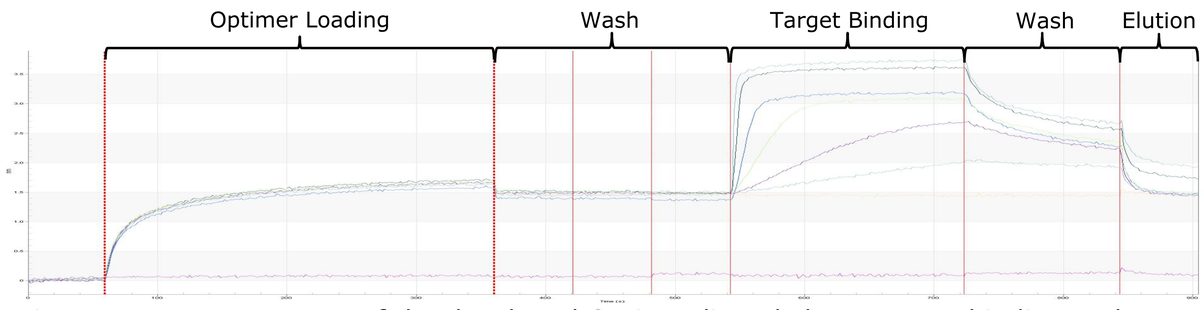

Figure 5: BLI assessment of the developed Optimer ligand shows target binding and elutions with a concentration-dependent response (K_D ~10nM).

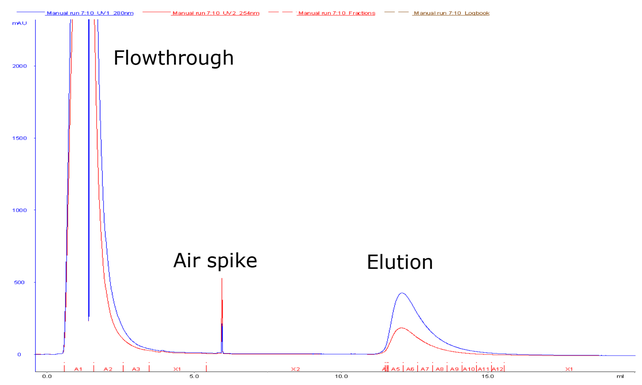

Figure 6: Small scale purification was demonstrated using an Optimer-functionalised column on an AKTA Explorer FPLC system.

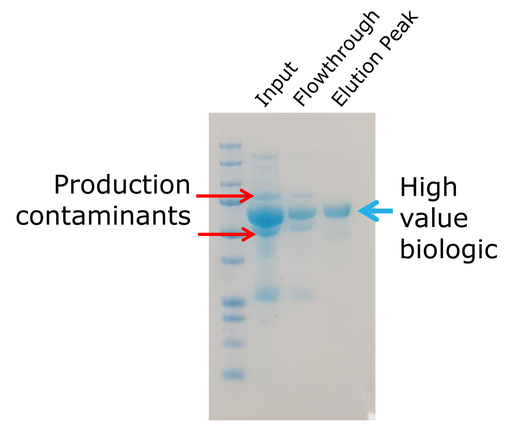

Figure 7: SDS-PAGE shows purification of the therapeutic protein target in a single pass, without the presence of the co-purifying contaminant species.

Case study 4: Optimer-based viral protein purification

- A single ligand was required for monolith chromatography of SARS-CoV-2 Spike (S) receptor binding domain (RBD), S trimer and S-virus like particles (VLPs).
- Optimer ligands to the SARS-CoV-2 S-protein subunit were developed in 17 days and showed successful purification of all three analytes from monolith columns enabling simplified purification processes across protein purification and viral-like particle purification.

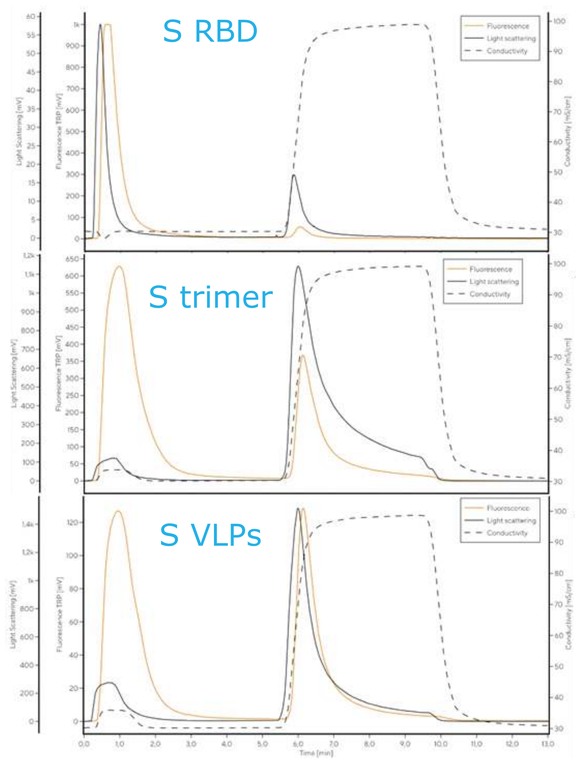

Figure 8: All three protein S analytes bind and elute from the Optimer column. MALS : fluorescence ratios show increasing sizes compatible with the expected sizes of the analytes (RBD < trimer < VLPs).

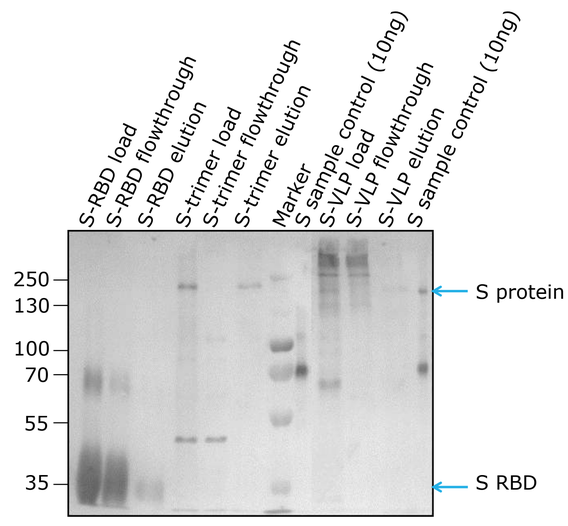

Figure 9: Successful purification of all three SARS-CoV-2 analytes (S RBD, S trimer and SVLPs) was achieved via Optimer-monolith chromatography.

Summary

- Optimer ligands have been successfully developed to novel therapeutic targets and to allow elution under specific conditions to retain protein function for improved yield and to remove contaminants from the end product.
- Optimer discovery offers the opportunity to incorporate multiple positive and negative selection steps into the discovery process and tune the binding and elution conditions of the developed affinity ligands to overcome challenges associated with alternative affinity ligands
- Batch consistent synthetic production, simple ligand functionalisation for resin compatibility and the rapid development of Optimer ligands in as little as four weeks, means Optimers are enabling new bioprocessing solutions.