

Optimizing Medium-Scale Protein Production Using Automation

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Introduction

The medium-scale protein production platform is critical for accelerating early-stage biologics development. By automating DNA transfer and transfection at 25–30 mL scale, the platform enables high-throughput protein production at the multi-milligram level.

We implemented and optimized Takeda’s proprietary production workflow using the 6 deep-well plate system, overcoming several limitations associated with traditional spin tubes. Integrated with the automation system, the platform increases throughput, supports high protein yields, and streamlines sample handling. This combination provides an efficient, scalable solution for antibody and antigen screening and downstream analysis.

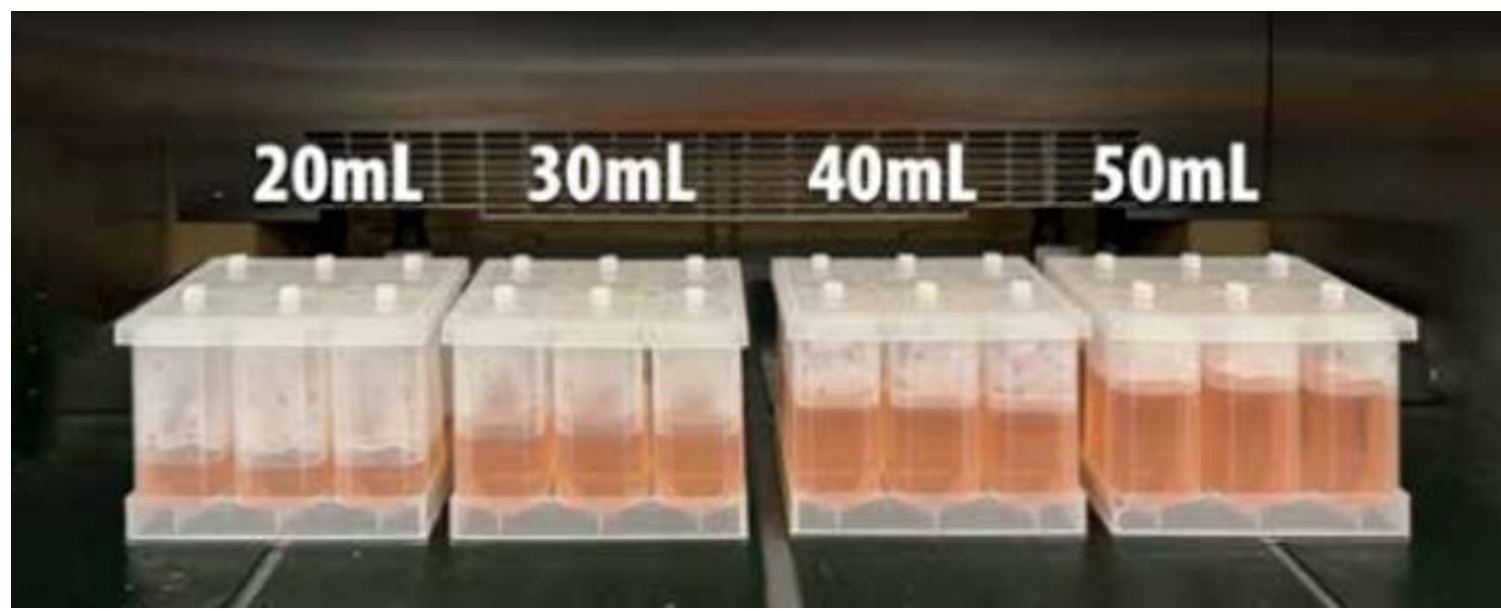


Figure 1: The 6 deep-well plate production platform accommodates working volumes of 20–50 mL per well (Image courtesy of Thomson Instrument Company).

Automating Medium-Scale Transfection

Medium-scale production is executed end-to-end under automation, encompassing DNA transfer, transfection, and feeding, with minimal operator intervention required.

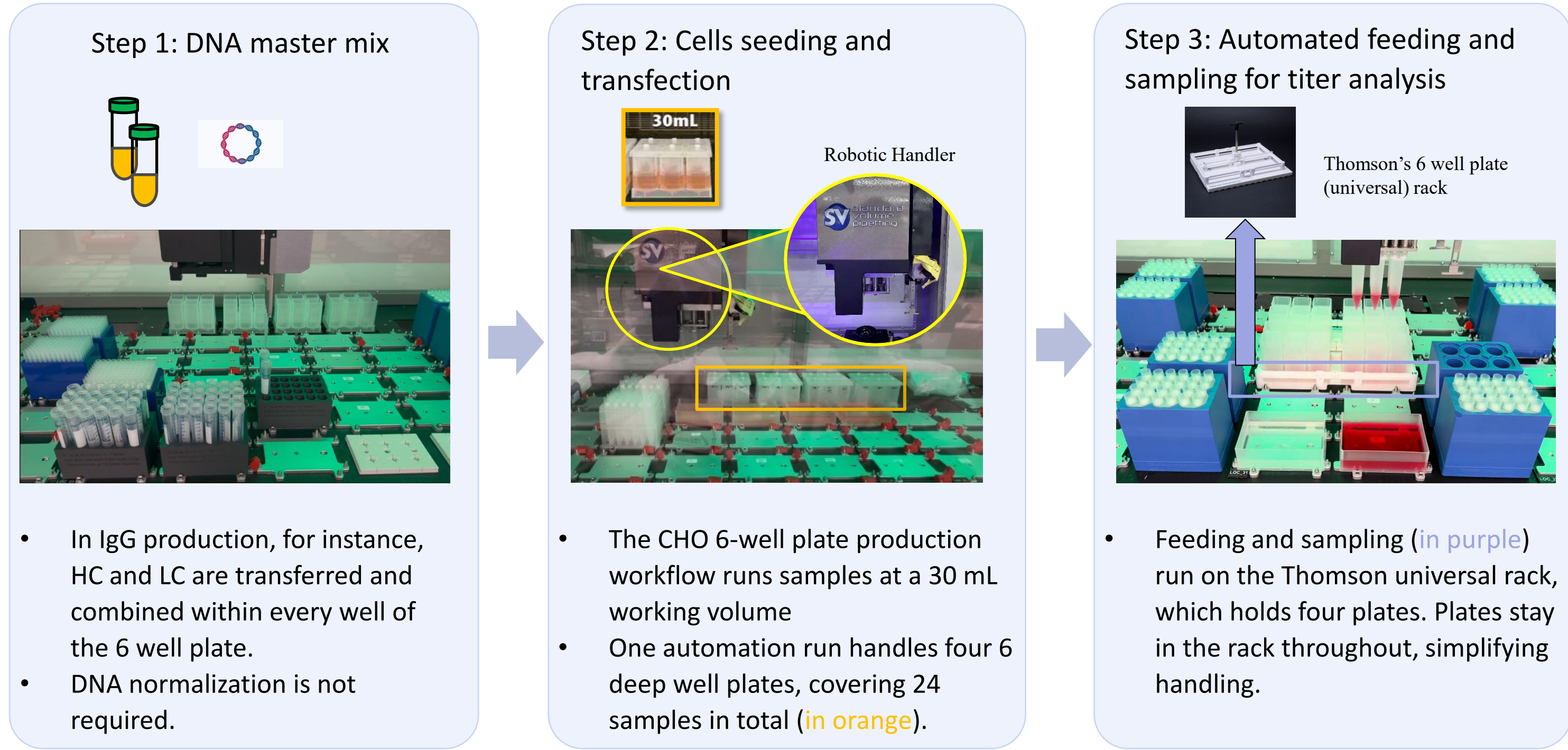


Figure 2: Lynx LMI1800 automation configuration supporting Takeda’s proprietary CHO cells production workflow

Clarification and Purification Workflows

Culture harvest following two steps purification processes

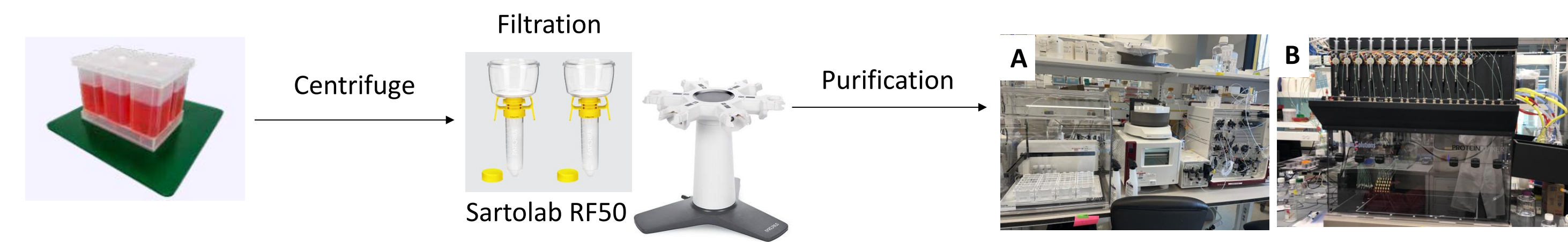


Figure 3: Methods of clarification and purification used with the 6 well plate production platform. Purification applied from automated workflows run on either CETAC-AKTA (A) or Protein Maker (B)

Table 1: Clarification workflow(s) specification

	Current workflow	Other workflow (in evaluation)
Method	Centrifuge + clarification using vacuum filtration with Sartolab® Multistation	6-well depth filtration called ProtoPress clarification using Lynx
Clarification vessel formats	50ml falcon tube	6 well plate
Notes	Manual method: transfer samples from 6 well plates to 50ml falcon tubes for clarification. Total time handling is ~15 mins.	Automation method: combining 30ml tips for samples transfer using Lynx and streamline for 6 well plate handling. One plate filtration time is shortened to 6 minutes only.

Table 2: Automated 2 steps purification processes comparisons between CETAC-AKTA and Protein Maker

	CETAC	CETAC	Protein Maker
Method	Capture-SEC	Capture-Desalting	Capture-Desalting
Production Scale	30-40ml	30-40ml	30-40ml
Average samples per day	9	12	48-96
Purity	High	Medium	Medium
Protein Yield	1-40mg	1-80mg	1-40mg
Final Buffer	User Choice	User Choice	User Choice

Conclusion and Acknowledgements

- The liquid-handling platform automates medium-scale transfection and feeding in 6-deep-well plates. This CHO workflow achieved titers above 1.6 g/L while sustaining cell viability through Day 7.
- The automation platform can be extended to clarification using the ProtoPress platform (in evaluation), providing an opportunity to seamlessly transition to protein purification.
- Overall, the results demonstrated efficient medium-scale protein production using an automated platform, enabling parallel processing of 24 samples in a single run.

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High-Capacity Automation Processes

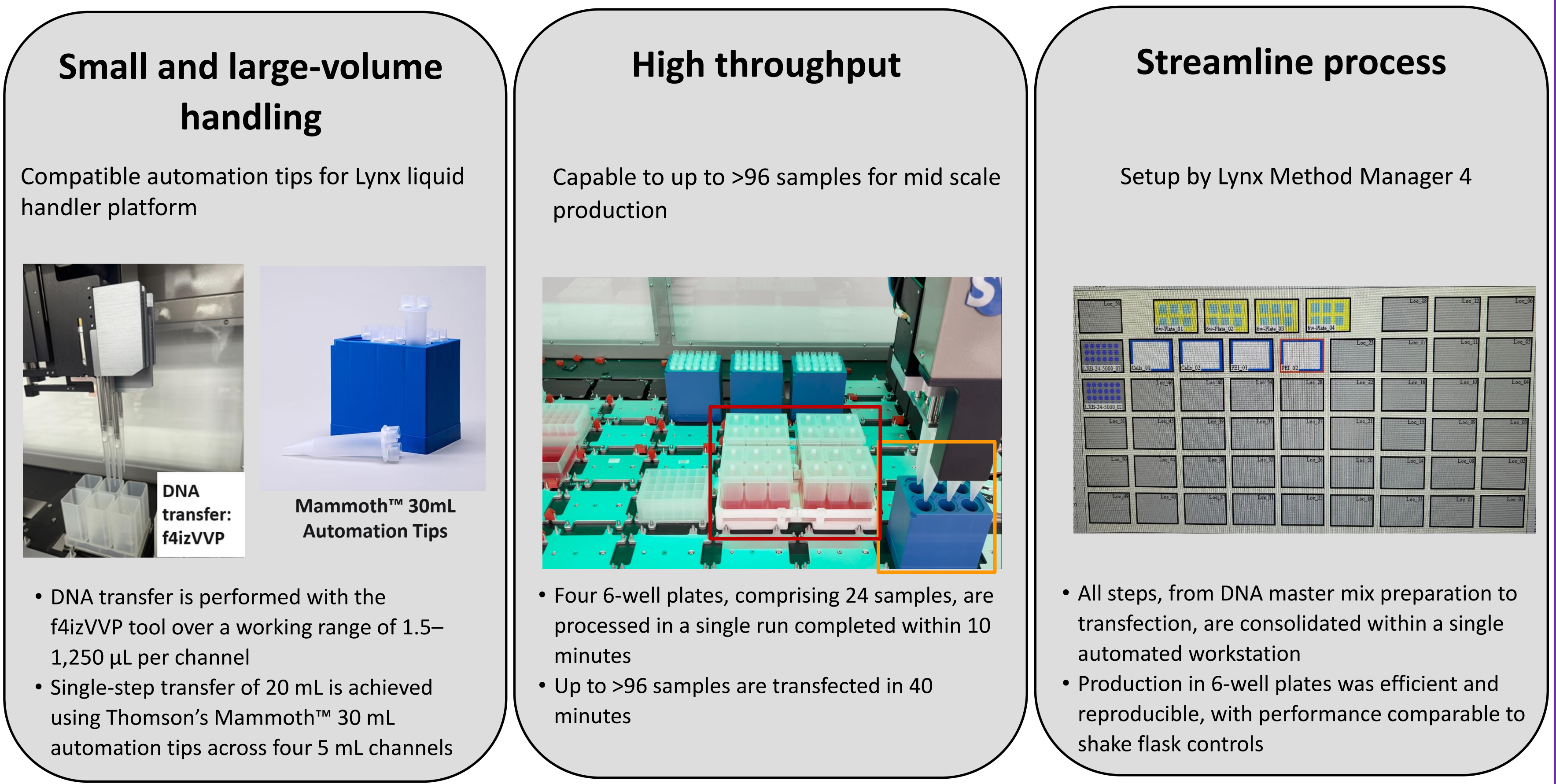


Figure 4: 6 well deep plate production platform enhancing midscale bioprocessing with larger volumes (20-50mL) through automation handling including 30ml tips, high throughput, reproducible results with streamline process.

Data

Automated medium-throughput expression of Target A and Target B– tool IgGs

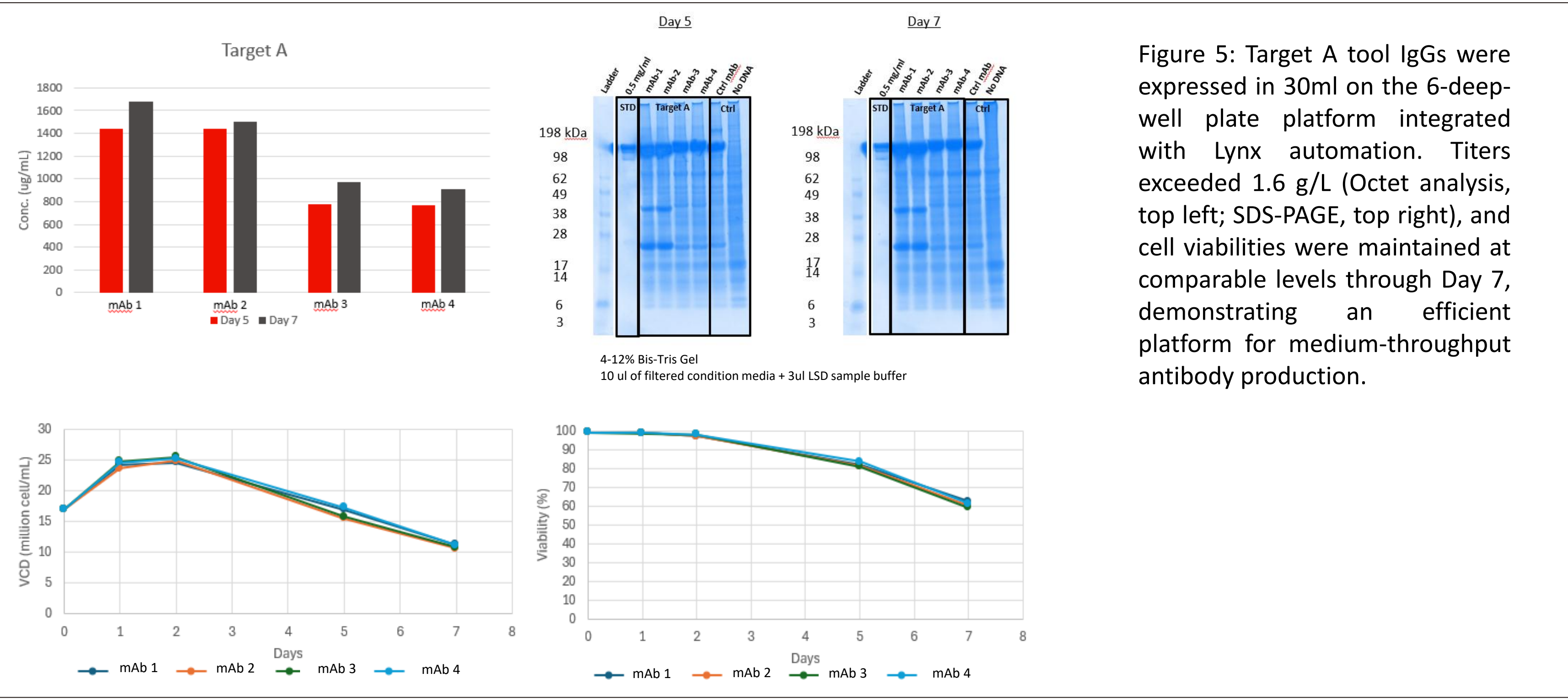


Figure 5: Target A tool IgGs were expressed in 30ml on the 6-deep-well plate platform integrated with Lynx automation. Titers exceeded 1.6 g/L (Octet analysis, top left; SDS-PAGE, top right), and cell viabilities were maintained at comparable levels through Day 7, demonstrating an efficient platform for medium-throughput antibody production.

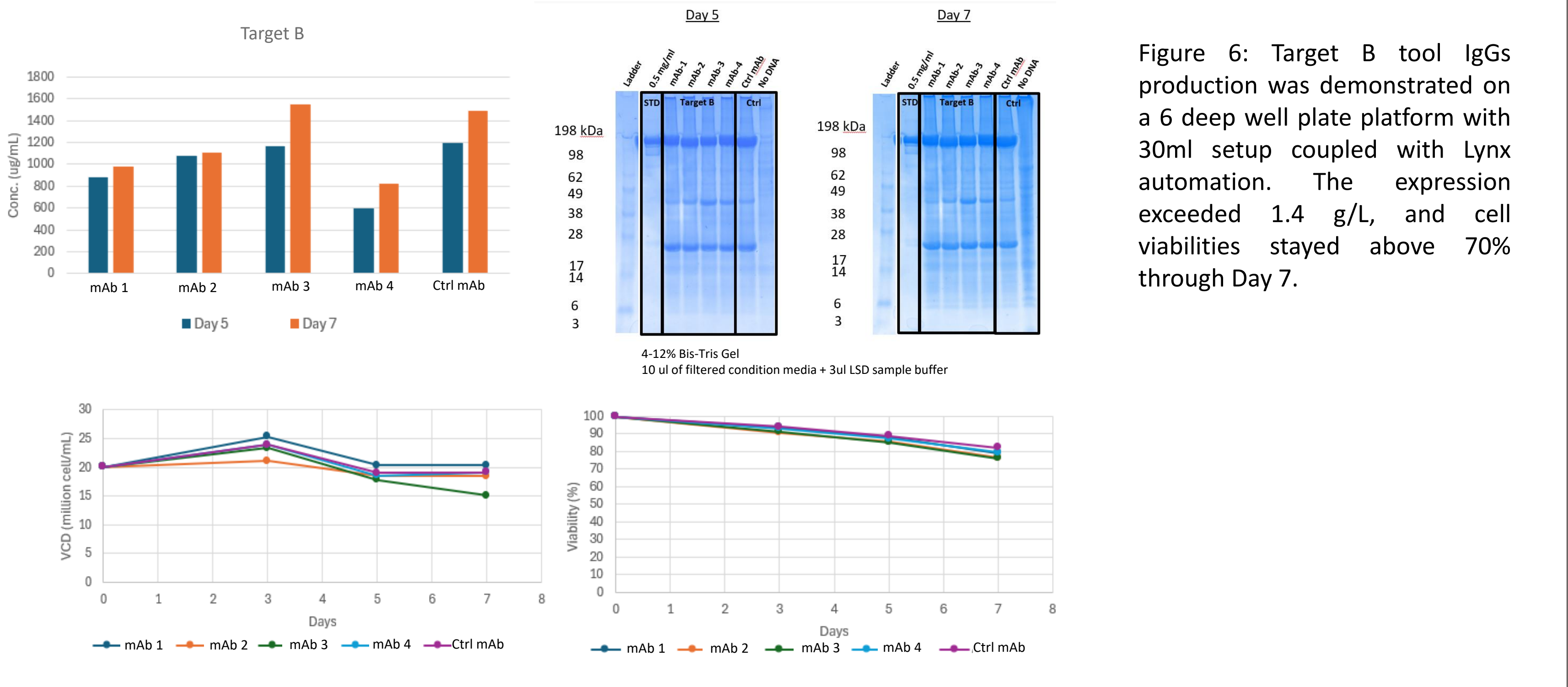


Figure 6: Target B tool IgGs production was demonstrated on a 6 deep well plate platform with 30ml setup coupled with Lynx automation. The expression exceeded 1.4 g/L, and cell viabilities stayed above 70% through Day 7.

Production in the 6 well plate achieved yields above 20 mg

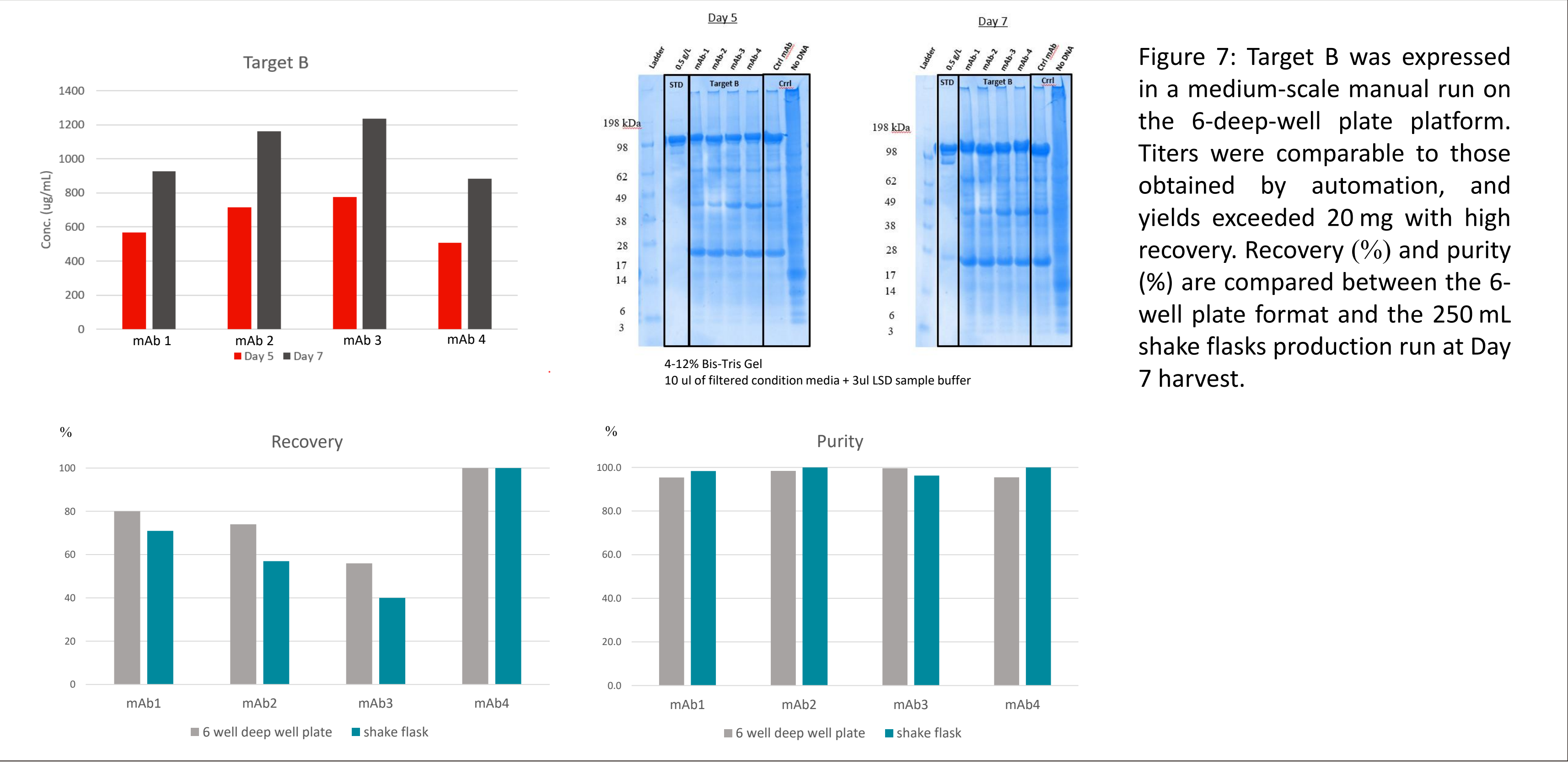


Figure 7: Target B was expressed in a medium-scale manual run on the 6-deep-well plate platform. Titers were comparable to those obtained by automation, and yields exceeded 20 mg with high recovery. Recovery (%) and purity (%) are compared between the 6-well plate format and the 250 mL shake flasks production run at Day 7 harvest.