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An integrated cell line development platform for generation of high yielding CHO stable cell lines expressing a stabilized trimeric pre-fusion RSV F recombinant viral glycoprotein

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AN INTEGRATED CELL LINE DEVELOPMENT PLATFORM FOR GENERATION OF HIGH YIELDING CHO STABLE CELL LINES EXPRESSING A STABILIZED TRIMERIC PRE-FUSION RSV F RECOMBINANT VIRAL GLYCOPROTEIN

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Key Words: RSV, trimer, pre-fusion.

Accelerating timelines to deliver stable cell lines with high productivity is challenging, especially for biologics portfolios which include complex recombinant vaccine constructs. The VRC's current integrated approach to shorten CHO cell line development timeline utilizes host cells pre-adapted to production medium, optimization of the expression vectors, improved pre and post-transfection methodology, automated ClonePix™ technology and top clone selection and ranking in micro-scale ambr bioreactor technology. This platform was developed with monoclonal antibodies as model proteins. While this integrated platform enabled generation of high yielding clones expressing monoclonal antibodies, it was initially much less successful with a difficult to express recombinant stabilized trimeric RSV F protein. Initial stable CHO cell lines produced the RSV F protein at very low levels that were not suitable for GMP manufacturing and the protein did not have quality attributes similar to the initial transient expression-based research protein. The RSV F trimer requires enzymatic cleavage of the protein for proper folding and trimer formation. However, the need for stable co-expression of a furin-like molecule in CHO cells was initially unknown. This case study summarizes the successful development of stable CHO cell lines expressing the stabilized RSV F trimer and a cell line development protocol for difficult to express trimeric viral glycoproteins for clinical manufacturing. Implications for cell line development of next generation trimeric HIV envelope vaccines will be discussed.

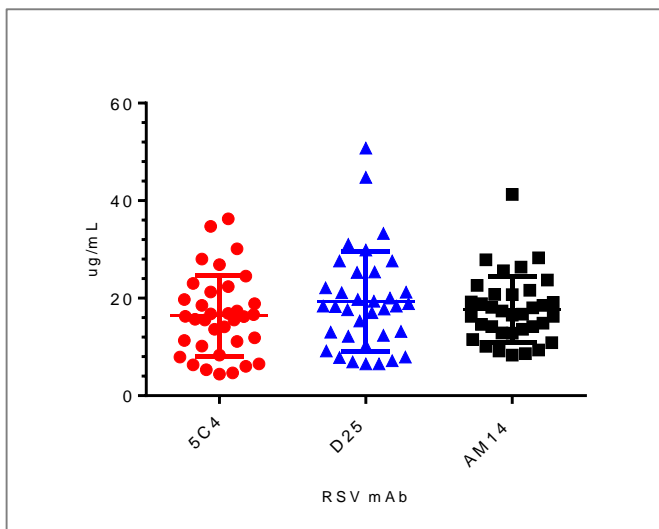


Figure 1. 7-day CHO batch shake flask harvest titer using three anti-RSV monoclonal antibodies

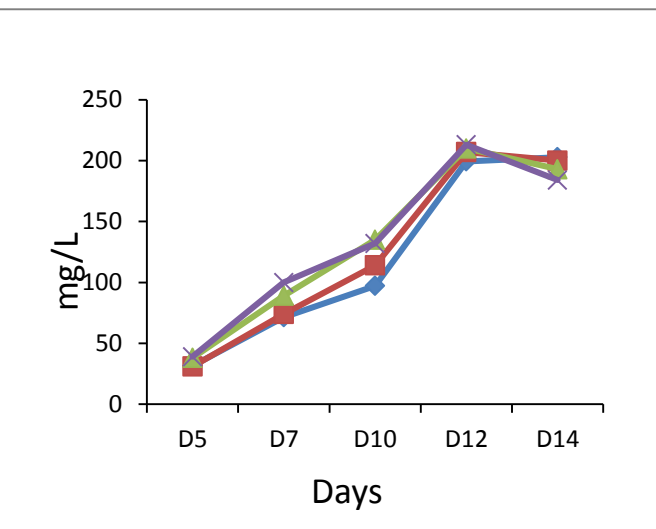


Figure 2. 14-day CHO Ambr fed-batch titer