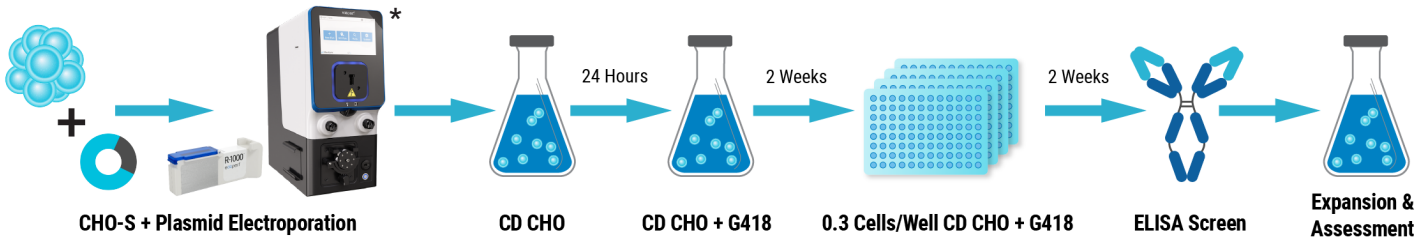
MaxCyte® Enables Rapid, High-Yielding, Stable Cell Line Development

Scientific Brief | Protein Production

Abstract

MaxCyte's highly efficient large-scale Flow Electroporation® has extended the potential use of transient protein production in CHO cells as a tool for both early and mid-stage biotherapeutic development. However, stable monoclonal CHO cell lines remain the system of choice for manufacturing clinical-grade biologics. Stable cell line development continues to be a bottleneck; a time-consuming, costly and labor-intensive process, often requiring specialized equipment. Here, we present a method for generating high-yielding stable CHO clones within six weeks of transfection.

Experimental Design



Electroporation

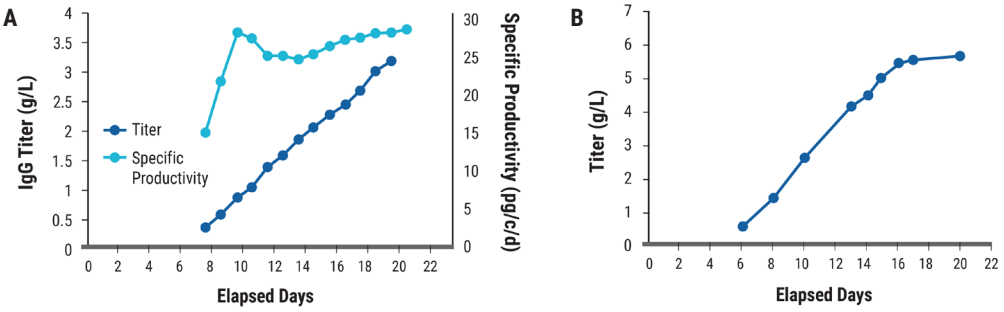
An IgG expression plasmid was added (1-2 µg DNA/10^6 cells) to CHO-S cells in MaxCyte electroporation buffer ($2x10^8$ cells/mL). Cells were transferred to a processing assembly and electroporated on the MaxCyte STX™ using the pre-loaded CHO program.

Culture and Selection

Cells rested for 30 minutes and were then seeded ($4x10^6$ cells/mL) in CD CHO (24 hours at 37°C). Cells were harvested via centrifugation and cultured in CD CHO with G418 for two weeks.

Limiting Dilution and Screening

Cells were seeded (0.3 cells/well) into 25 x 96-well plates in CD CHO with G418 for two weeks. 479 clones were screened by ELISA. The 23 top-producing candidates were expanded in shake flasks. Productivity was assessed up to day 21 of culture.



The top-performing clone, identified within six weeks, was examined for yield and stability. A) In unoptimized culture conditions, specific productivity reached 27 pg/cell/day and remained high over the 21-day production period, when the final antibody titer reached 3.4 g/L. B) With process development, including optimized media/feed strategy, titers exceeded 5.7 g/L.

Summary

- MaxCyte enables rapid, simple, cost-effective CHO-S stable cell line development within six weeks of electroporation.
- High transfection efficiency and cell viability eliminate the need to screen thousands of candidate clones.
  - Lower consumable costs
  - Less hands-on time
- Simplified development with limiting dilution cloning directly from a stable bulk pool.
  - Avoid multiple rounds of subcloning and screening
  - No need for specialized equipment
- Large-scale electroporation of up to $2x10^{11}$ cells enables multi-gram transient protein expression in parallel with stable cell line development.

Steger K, Brady J, Wang W, Duskin M, Donato K, Peshwa M. CHO-S antibody titers >1 gram/liter using flow electroporation-mediated transient gene expression followed by rapid migration to high-yield stable cell lines. J Biomol Screen. 2015 Apr; 20(4):545-51. Copyright (2015) with permission from Elsevier.

* Since the publication of this study, the new ExPERT STx® instrument has been released to include enhanced software, an improved user interface and an integrated touch screen.

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