

Rapid Selection of Optimal Formulations for Divergent Clones Through Screening Chinese Hamster Ovary Media Library

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ESACT 2007 Poster#XXXX

Abstract

The successful culture of Chinese Hamster Ovary (CHO) cells can be a challenging endeavor. Historical data shows that CHO clones have diverse nutritive requirements. Selecting a medium designed specifically for a CHO cell line is a key component for achieving optimal growth and productivity. With the wide variety of media available, narrowing the number of formulations for screening can be time consuming and can impede the development process. After screening a battery of media, we have narrowed the field to a finite collection of formulations under the classification of the SAFC Biosciences' CHO Media Library. Each of the formulations found within the CHO Media Library have been chosen for their ability to meet the divergent needs of numerous CHO cell lines, including DUX B11, CHO-K1 and CHO-S. The majority of these formulations have a proven track record in industrial applications and the data shows that, with or without adaptation, several formulations can be quickly selected for further investigation after performing a growth assay using the library. Performance of each formulation is evaluated based on: peak cell density, integrated cell days, viability, culture longevity and, where applicable, volumetric productivity. Most offerings in the library are free of animal-derived components while others are truly chemically defined (CD).

Introduction

SAFC Biosciences (SAFCB) has a diverse collection of cell culture formulations for use with CHO cells. Previously, as cell lines arrived for media development, there was no specific subset of media for screening. While leading to the creation of many successful media formulations, this method had the possibility of omitting formulations with better potential. After testing multiple cell lines in the vast array of SAFCB media, the best possible subset has been labeled the CHO Media Library. This current selection of media allows a more consistent starting point for new media screening projects.

Materials and Methods

Cell lines and media

The CHO cell lines tested with CHO Media Library were CHO-S (Invitrogen) and a recombinant CHO-S line that produces human IgG. The CHO-S stock culture was maintained in Gibco CD CHO Medium (Invitrogen) while the recombinant CHO-S line was cultivated in a proprietary animal-component free formulation. All SAFCB and competitor media were supplemented with 4 mM L-Glutamine. Cultures were inoculated directly from stocks into TPP™ 50 mL bioreactor tubes containing the applicable formulations for testing. Each condition was assayed in duplicate and averaged.

Productivity assay

Human IgG: IgG concentrations were measured by Protein G affinity chromatography.

Results

CHO Media Library Screening

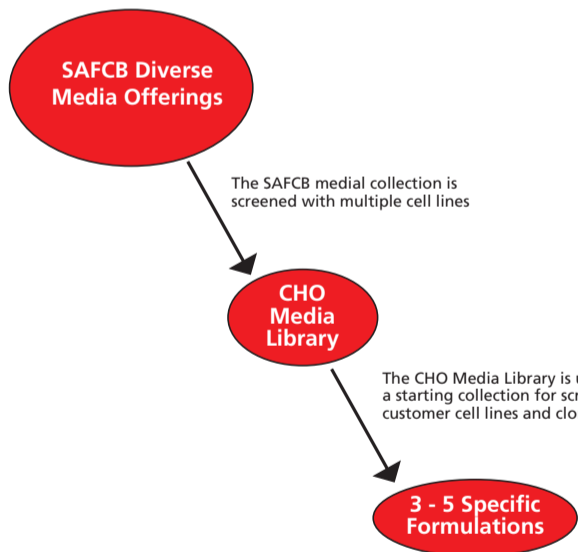


Figure 1: Multiple CHO cell lines were screened with the diverse CHO media formulations available from SAFC Biosciences. The best of these formulations have been designated the CHO Media Library. This collection constitutes a starting point for incoming screens of customer CHO clones. The screen allows for the identification of the best 3 – 5 formulations for a specific clone or group of clones.

Screening growth assays on CHO-S and the recombinant CHO-S cell lines using the CHO Media Library

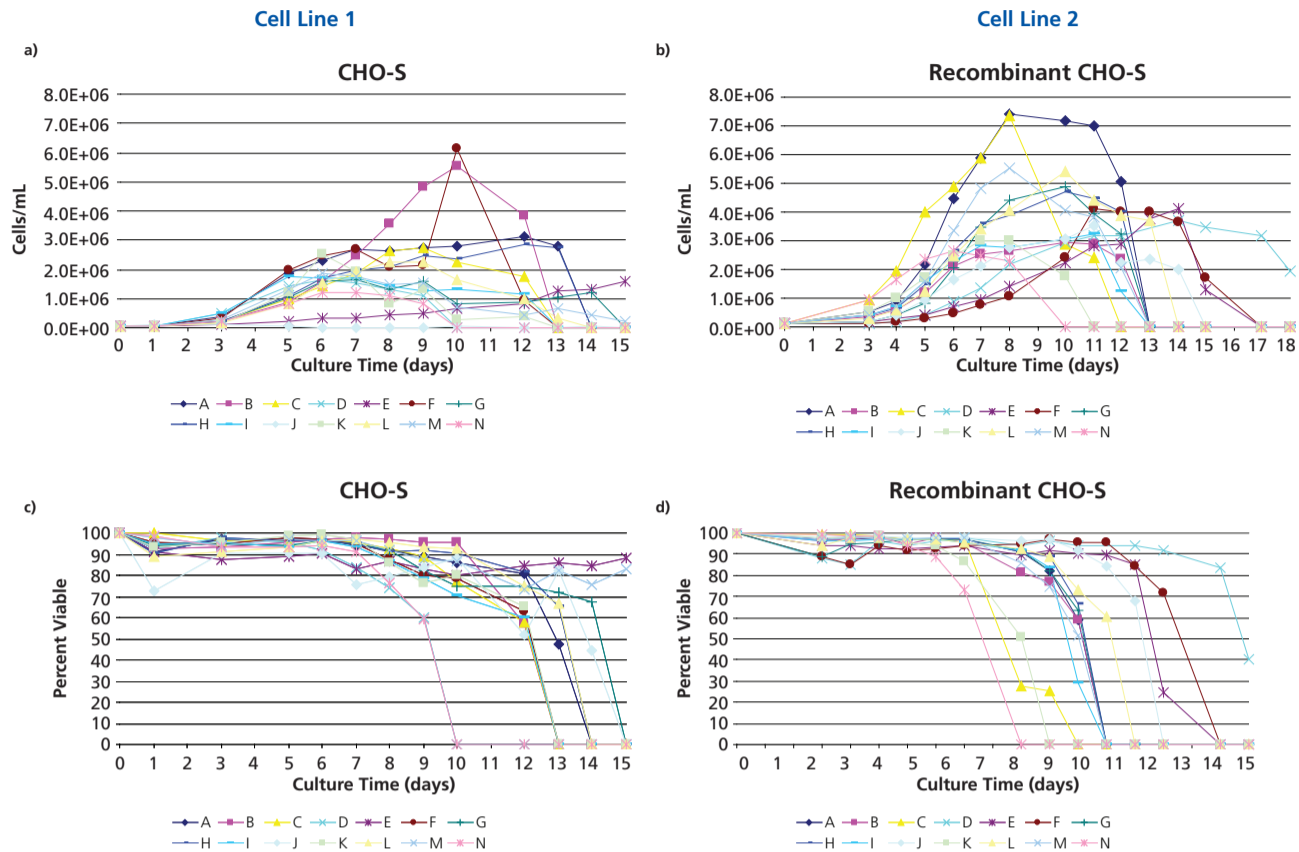


Figure 2 a & c: Cell Line 1 - Parental CHO-S

Figure 2 b & d: Cell Line 2 - Recombinant CHO-S

By evaluating the cell density and viability curves, the differences can be seen in the peak cell density and longevity of the cultures. For cell line 1, formulations F, B and A have the best growth, respectively, based on peak viable cell density. For cell line 2, the best growth is seen in formulations A, C, M and L. These differences in media preference illustrate the distinctions between the parental CHO-S line and the recombinant CHO-S line.

IgG-producing recombinant CHO-S cell line screened in CD formulations from the CHO Media Library and competitors

SAFCB Formulations

Competitor Formulations

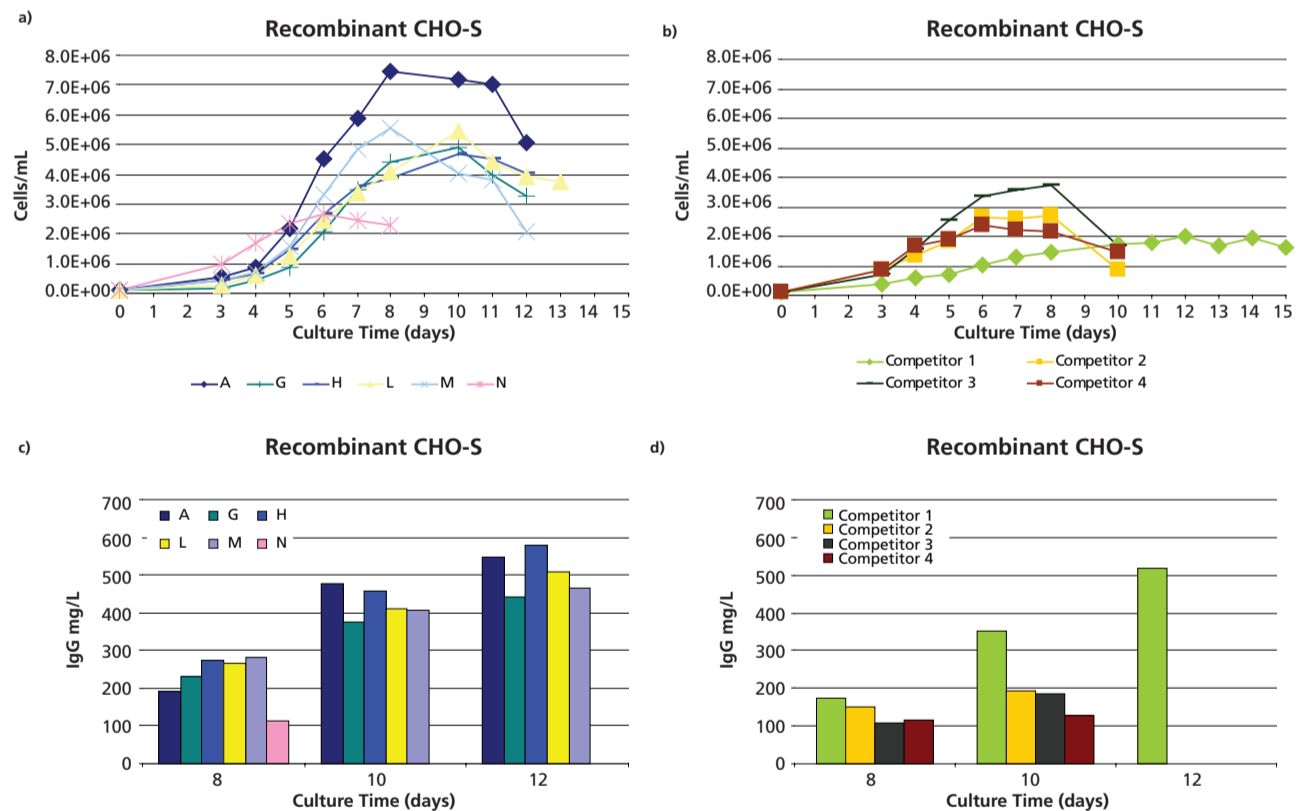


Figure 3 a & c: CHO Media Library

Figure 3 b & d: Competitors

When comparing CD formulations from the CHO Media Library with those available from competitors, there is a range among the peak viable cell densities and volumetric productivity. Also evident is the distinction between formulations that promote good growth versus ones that promote higher productivity.

Conclusions

- SAFC Biosciences has a wide range of media that has been narrowed to a collection called the CHO Media Library which serves as a starting point for screening customer CHO cell lines.
- Based on assay parameters (i.e. peak cell density, viability, longevity and productivity), the best performing formulations are defined for a specific cell line.
- A full screen of the CHO Media Library is suggested, even when the parental cell line is known, because a recombinant cell line may have a distinct preference for alternate formulations.
- When the offerings from the CHO Media Library are screened against competitor formulations, the diversity among the formulations is further amplified by the differences in growth promotion and volumetric productivity.