

The evolution of CHO cells' role in cell line development

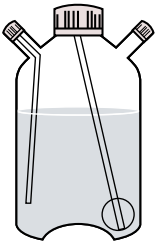
Since the first approval of recombinant insulin and human growth hormone in the early 1980s, a multitude of recombinant protein therapeutics have been approved by regulatory agencies, notably the FDA in the US and EMA in Europe. Given this significant increase in successful introduction of biological therapeutic agents, there is a crucial need in the drug discovery space to support more efficient manufacturing processes that require highly productive cell lines. Consequently, Chinese Hamster Ovary (CHO) cells have emerged as the gold standard for the manufacturing and regulatory approval of therapeutic proteins.

Why CHO?

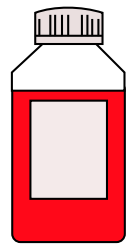
Several key properties of CHO cells have driven their establishment as the preferred host cell line for regulatory approvals of recombinant therapeutic products:

- 1**

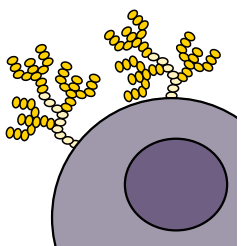
Adaptable to growing in suspension culture, which is ideal for large scale production in bioreactors.


- 2**

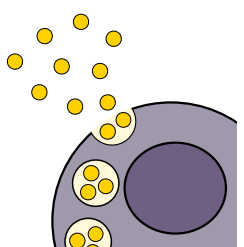
Adaptable to growth in serum-free and chemically defined (animal-free) media supplements, which ensures reproducibility between different batches of cell culture.


- 3**

Allow posttranslational modifications (e.g. glycosylations) to recombinant proteins which are compatible and bioactive in humans.


- 4**

Several chemical selection and gene amplification systems have been developed for CHO cells, optimized for higher yield of recombinant protein per cell.



CHO-ori

CHO cell line is established in the laboratory of Theodore Puck at the Eleanor Roosevelt Institute for Cancer Research. CHO-ori cells actively divide and do not exhibit the limitations on doubling times (Hayflick Limit) observed in primary cells.

CHO-S

Adapted for growth in suspension liquid culture, this cell line is ideal for scale up and growth in large-scale bioreactors.

MTX-Induced Gene Amplification

An approach was proposed to amplify genes with the help of an antagonist of DHFR, the chemical component methotrexate (MTX). Selection of recombinant cell lines using stepwise increases in the MTX concentration in the culture medium resulted in amplified copies of the transfected DHFR gene together with the GOI. Such induced gene amplification usually increased the productivity of the GOI.

Activase® is approved by FDA

Human tissue plasminogen activator, marketed as Activase® (Genentech) becomes the first therapeutic protein from recombinant mammalian cells to obtain market approval.

CHO-K1SV

Vectors for the Glutamine Synthetase (GS) system, first reported in 1987, were adapted to the CHO cell line.

CHO-K1

Kao, Puck and co-workers cloned the CHO-ori cells and distributed to collaborators. Mutational analysis of CHO-K1 suggests that this cell line is missing a chromosome which carries a gene necessary for glycine biosynthesis, paving the way for selection methods utilizing chemicals components in media.

CHO-DXB11

Urlaub and Chasin at Columbia University generated CHO lacking DHFR activity in one locus and a missense mutation in the other. DHFR-deficient strains cannot grow unless transfected with a functional copy of DHFR or in media supplemented with thymidine. Thus, transfecting DXB11 cells with a functional DHFR gene attached to a gene of interest (GOI) enable selection of cells only carrying their GOI by growing them in thymidine-free media.

CHO-DG44

Urlaub and Chasin constructed a CHO line containing full deletion of the two DHFR loci. DXB11 cells were limited in their usefulness because they could spontaneously revert back to a functional DHFR enzyme, making selection impossible. CHO-DG44 eliminated this problem by completely deleting the DHFR locus, making selection for the GOI always possible. Due to this, CHO-DG44 are amongst the most widely used CHO cells for industrial protein production.

Today...

More than 100 new recombinant protein therapeutics have been approved by the US FDA or the EMA. With the increased interest in viral diagnostics and treatments, CHO cells are again demonstrating their versatility. They are being engineered to express coronavirus antigens in the quest to develop new vaccines, and they are being used to produce monoclonal antibody therapeutics that may provide new treatments for COVID-19.

Cell line development can be time-consuming.

Accelerate the discovery with our products:

CHO Growth A

Liquid and semi-solid culture media specifically for CHO cells



ClonePix 2 System

Automated clone screening and picking system



CloneSelect Imager

Imaging system to track and confirm monoclonality

