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.

MILESTONES

1956 — 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.

1968 — 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.

1971 — CHO-S

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

1980 — CHO-DXB11

Urlaub and Chasin at Columbia University generated CHO lacking DHFR activity in one locus and a missence 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.

1981 — 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.

1983 — 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.

1986 — 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.

1989 — CHO-K1SV

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

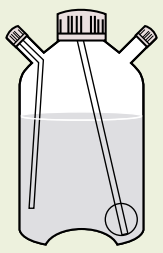
2000s — Today...

More than 100 new recombinant protein therapeutics have been approved by the US FDA or the EMA.

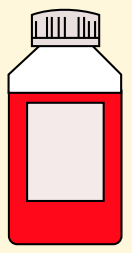
WHY CHO?

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

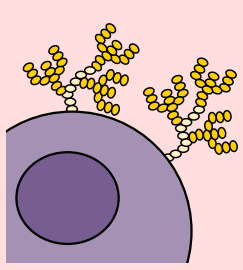
1 Adaptable to growing in suspension culture, which is ideal for large scale production in bioreactors.



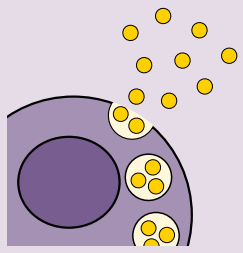
2 Adaptable to growth in serum-free and chemically defined (animal-free) media supplements, which ensures reproducibility between different batches of cell culture.



3 Allow post-translational 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.



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