



Harness the power of UCOE technology with the experience and expertise of Cobra Biologics' cell line development team including the Cello™ robotic system.

Features and Benefits

- Enables rapid production of gram quantities of recombinant proteins
- Ensures efficient expression independent of chromosomal location
- Evaluated for recombinant antibodies, secreted and intracellular proteins
- Eliminates the need to screen thousands of clones
- Unique mechanism that prevents gene silencing through effects on chromatin structure
- Purified mixed pool material in 10 weeks
- Vectors are *de novo* synthesised and fully sequenced

open chromatin show efficient expression of the transgene.

Ubiquitous Chromatin Opening Elements (UCOE) have been isolated which ensure efficient expression in a wide range of cell types including CHO-K1, CHO-S,

HeLa, and NS0 cells. UCOE containing vectors have been shown to markedly enhance a wide variety of intracellular, secreted and membrane-bound proteins.

Inclusion of a UCOE (4-8 kb in size) in a eukaryotic expression vector permits efficient expression in the vast majority of stable clones, whereas with conventional vectors, only a minor proportion of transfectants show high-level expression (Figure 1).

Application

Rapid and high-yielding production of correctly folded and glycosylated proteins: Antibodies, Therapeutic recombinant proteins, Vaccines and Diagnostics:

- Antibodies
- Therapeutic recombinant proteins
- Vaccines
- Diagnostics

How UCOEs work

Eukaryotic genes are organised into chromatin domains, which exist in either a 'closed' state in which the genes are tightly condensed with proteins and are transcriptionally silent, or in an 'open' de-condensed state: a prerequisite for efficient gene expression.

When transfected genes integrate into mammalian chromosomes, the structure of the chromatin at the site of integration has a profound effect on expression of the transgene. Consequently, only relatively rare transfected clones where the expression vector has integrated into

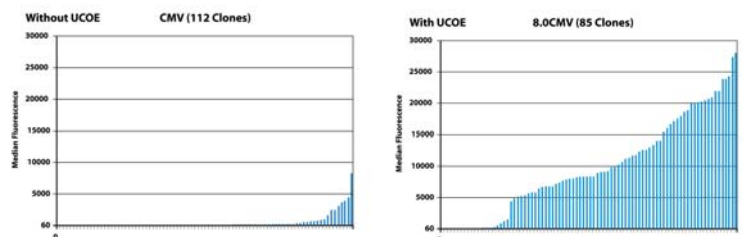


Figure 1: CHO cells stably transfected with a human CMV-EGFP reporter gene combination with, or without, an upstream 8kb UCOE. Median fluorescence indicates the level of expression of the reporter gene achieved in individual clonally derived transfectants.

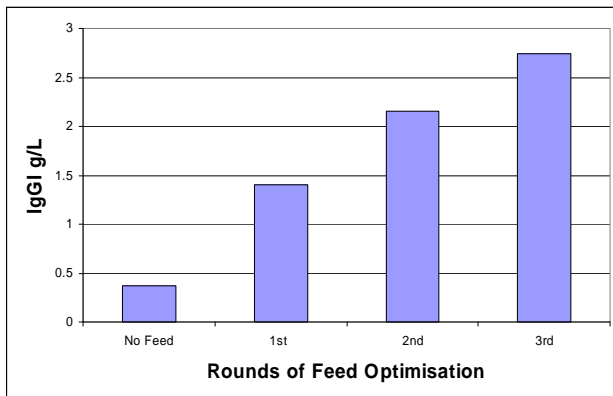


Figure 2: High IgG1 yields can be obtained with Feed optimisation.

There is therefore no need for amplification and expression has been demonstrated to be stable over 130 generations. The combination of UCOE and CHO-S allows the generation of high yields of recombinant proteins (Figure 2).

Automated Cell Line Development

- Cello™ robotic system for automated screening and expansion of large numbers of clones after transfection or limiting dilution in 96, 24 and 6 well plate formats.
- Visual clone detection using image processing.
- Computerised data management:
 - Traceability of on-line (growth, clonality)
 - Off-line (titre) data
- Software generated tracking report covering:
 - Expansion
 - Selection
 - Pictures of clones in wells
 - Applicable to suspension cell based expression systems

Mammalian Cell Protein Services

Cobra Biologics, with locations in Matfors and Södertälje, Sweden and Keele, UK, provides a full range of services from gene cloning to cGMP manufacturing including fill/finish for pivotal pre-clinical through to Phase III clinical trials.

Cobra Biologics' solid track record in manufacturing cGMP products helps to ensure programs are on time and to budget. Our goal is to accelerate our customers' protein development programs in a cost effective and timely manner.

- Cell Line Development
- Process Development & Scale Up
- Analytical Development & Qualification
- cGMP Manufacturing
- Fill/ Finish
- Quality Assurance & Regulatory Support

Quality Assurance & Regulatory Support

- Two Qualified Persons (QP)
- Fully compliant with European Clinical trials Directive 2001/20/EC and FDA standards
- Licensed for cGMP manufacture in Sweden and the UK
- Support customer with their CMC filings
- Representation at MHRA and FDA meetings
- QP release & Shipment to clinical trial sites

Fill/ Finish

- Aseptic production
- Syringes and vials
- Freeze drying/ lyophilisation
- Up to commercial scale
- Regular process updates and risk management

Project Management

- Dedicated Project Manager
- Cross-functional project teams
- Detailed timeline planning and milestone tracking
- Program managed by single point of contact
- Regular process updates and risk management