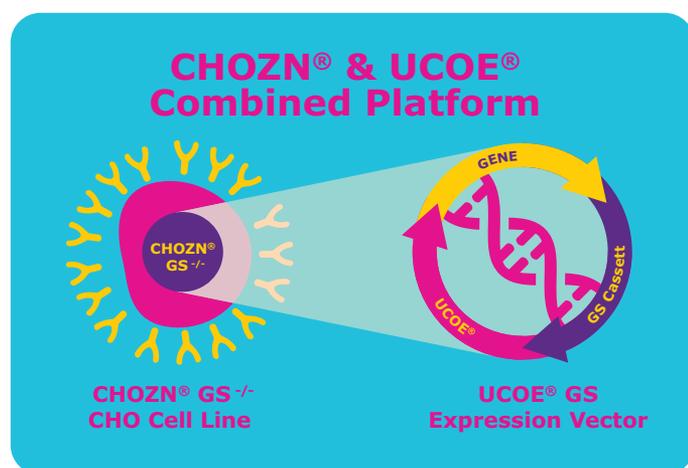


CHOZN® & UCOE® Combined Platform

Accelerate Biopharmaceutical Development with an
Integrated Upstream Solution



Isolate more high-producing clones with fewer resources

The CHOZN® & UCOE® Combined Platform's streamlined processes offer numerous efficiencies for cell line development. While maintaining all the benefits of the CHOZN® GS expression system, through the CHOZN® & UCOE® Combined Platform you can also:

- Accelerate your cell line development by increased efficiency of isolating high producing clones. Eight-fold more clone candidate pools and twice the number of clones expressing more than 3 g/L were obtained with the combined platform.
- Increase cell line development success with hard-to-produce molecules

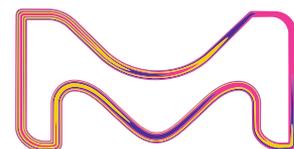
- Achieve high and stable titers to expedite your cGMP manufacturing with fewer resources

For nearly a decade, the CHOZN® GS platform has been used to develop high expressing, stable biomanufacturing clones. Consisting of a ZFN-modified CHO-K1 line, paired cell culture media and feeds, an expression vector, documentation and protocols, the platform is optimized to consistently isolate the high-expressing clones within a transfected pool. However, cell line development can be a lengthy and resource-intensive task because these high-expressing clones are relatively infrequent within the pool.

The UCOE® technology offers a path to increase the frequency of these high-expressing clones, thereby reducing the time and resources needed for cell line development.

The UCOE® (Ubiquitous Chromatin Opening Elements) technology uses naturally-occurring sequences capable of creating and maintaining open chromatin to enable high, stable transgene expression, regardless of the integration site. When included in a plasmid alongside the transgene of interest, these UCOE® elements greatly increase the number of high expressing clones that can be isolated within a single cell line development process.

To demonstrate the ability of the CHOZN® & UCOE® Combined Platform to increase the number of high-expressing clones, two concurrent IgG1 cell line development procedures were initiated. CHOZN® GS^{-/-} cells were transfected with either the standard CHOZN® GS expression vector containing gene cassettes



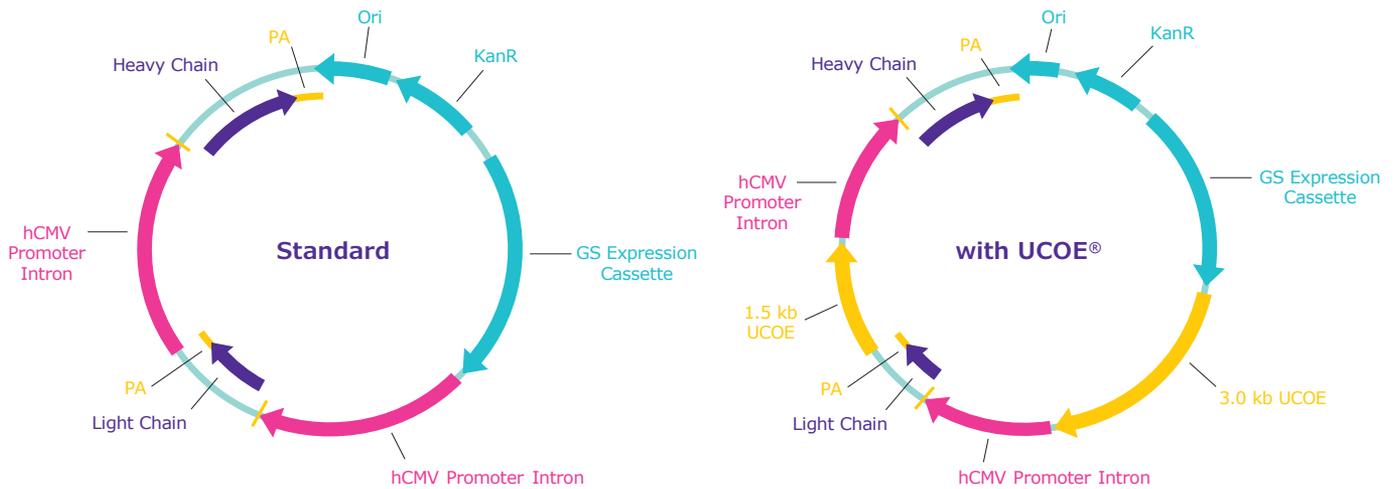


Figure 1. Standard CHOZN[®] expression vector (left) and CHOZN[®] expression vector with the addition of UCOE[®] sequences (right).

for an IgG1 heavy and light chain (Control), or the CHOZN[®] expression vector with the addition of UCOE[®] sequences (UCOE), pictured in **Figure 1**. The CHOZN[®] GS^{-/-} protocols were followed. At each screening step, the UCOE conditions yielded multi-fold more high producing pools and clones (Figure 2). This increased efficiency in generating high producing pools and clones in the CHOZN[®] & UCOE[®] Combined Platform can be leveraged to:

- Reduce screening and scale-up efforts over the course of cell line development without compromising productivity goals
- Help ensure cell line development success with hard-to-produce molecules
- Identify more pools and clones that match both titer and protein quality criteria

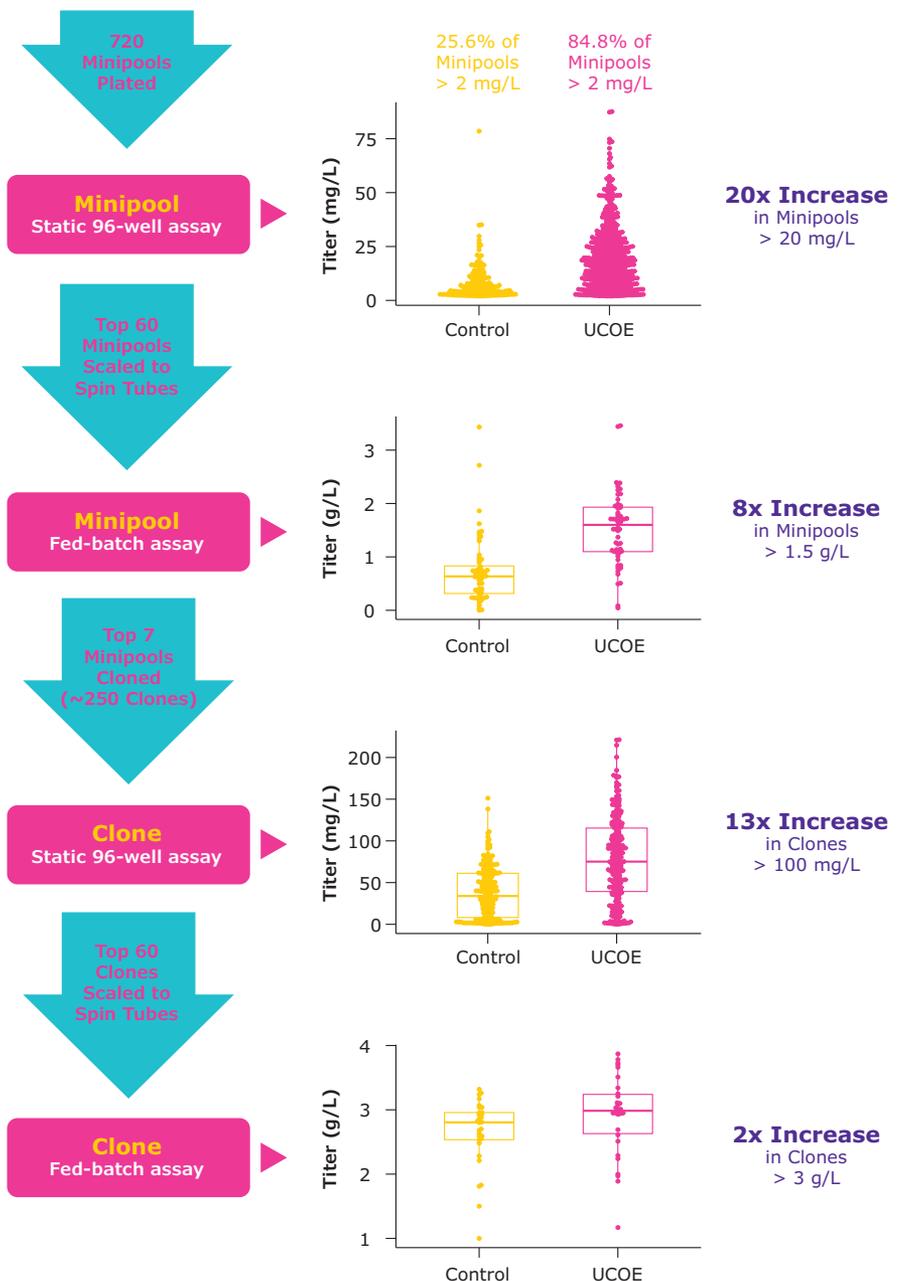


Figure 2.

At each screening step, the UCOE conditions yielded multi-fold more high producing pools and clones.

CHOZN® GS^{-/-} Cell line

- ECACC CHO K1 origin, adapted to suspension growth in chemically defined, animal component-free media
- GS^{-/-} phenotype knock out by targeted mutagenesis using the non-virus ZFN gene editing technology
- Enables rapid cell line development by metabolic selection without the addition of MSX (GS inhibitor)
- cGMP-banked and fully traceable cell lines
- Paired, batch-to-batch consistent and chemically defined cell culture media and feeds using highest grade of critical raw materials

UCOE® Technology

- Highly-characterized Ubiquitous Chromatin Opening Elements create and maintain open chromatin
- Offers major improvements in gene expression in stably transfected mammalian cells

CHOZN® & UCOE® Combined Platform

- Clear IP path for the complete platform
- Complete documentation and cell line history
- Comprehensive user protocols guide customers from transfection through small scale bioreactors
- Optimized UCOE® GS vector for expression of antibodies, Fc-fusion or recombinant proteins
- Simple and accessible combined platform licensing structure
- Technical support and consultation

To place an order or receive technical assistance in Europe, please call Customer Service:
France: 0825 045 645 Spain: 901 516 645 Option 1
Germany: 069 86798021 Switzerland: 0848 645 645
Italy: 848 845 645 United Kingdom: 0870 900 4645

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