Cell Line Development

Selexis SURE Cell Line Development™

SERVICES

SELEXIS

Selexis SURE Cell Line Development™

Proprietary technology platform and comprehensive services for fast and reliable cell line development:

- From DNA to IND in 14 months
- Highly adaptable non-viral vectors with no carrying capacity limitation
- No gene amplification required
- Single site of integration in the host cell genome
- No endogenous genes disruption
- Novel high-througput approach to address product-specific expression bottlenecks
- Validated track record in the expression of monoclonal antibodies, enzymes, Fc Fusions, GPCRs, ion channels…
- Full cell line data package including detailed vector information, host cell line pedigree, complete cell line documentation ready to use for IND filling
- Host CHO cell line genome fully sequenced enabling the precise mapping of the transgene integration site
- World class science, project management and highly efficient tech transfer to production facilities

HIGH PERFORMANCE

Single site integration in the host cell genome reduces the risk of endogenous genes disruption for unmatched stability and grams per liter productivities

RAPID DEVELOPMENT

High performance Selexis SUREclones™ in 15 weeks

TRANSFER

Selexis SUREclones™ with Selexis SUREfeed™ strategy transferred to CMO

Based on the Selexis SUREtechnology Platform™ and world-class expertise, Selexis SURE Cell Line Development™ Services significantly reduces the time, effort, and costs associated with developing high-performance mammalian cell lines for therapeutic protein production (i.e. monoclonal antibodies, growth factors, enzymes).

The development of high-yield production cell lines begins with the cloning of target genes into the SUREtech Vectors™ containing Selexis Genetic Elements™ (SGEs). These target gene-containing vectors are transfected either into the Selexis SURE CHO-M Cell Line™ or another fully documented cell line provided by the client using the SUREfection™ procedure. From the stable transfectant population Selexis selects for high expressing populations with favorable growth characteristics. If necessary, single cell cloning can be carried out to generate clonal populations with even higher protein expression levels.

Selexis SURE*technology* Platform™

• Clone Selection
• Expansion

Candidate Clones
- Productivity assay
- Fuctional assay
- Manufacturing
- Preclinic/tox

Clonal Cell Lines
- Media/feed optimization
- cGMP manufactuing
- Clinical trial supply
- Market supply
- Research cell bank

Generation of high performance and stable cell lines using the SURE*technology* Platform™ for cGMP manufacturing:

- ✓ Strong expression vector
- ✓ High-performance host cell
- ✓ Full chemically defined medium – NO SERUM OR OTHER ADC
- ✓ Feed strategy

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SURE Cell Lines At A Glance

SPEED
- 3 weeks for Selexis SURE*pools*™,
- 15 weeks for Selexis SURE*clones*™

HIGH YIELD
- 1-5 g/L for MAbs
- Increase in recombinant protein expression levels by up to 20 fold

STABILITY
- Stable expression of therapeutic recombinant proteins for more than 60 generations
- Single site integration
- Not associated with chromosomal rearrangements nor chromosomal breaks

FLEXIBLE
- Very effective in a variety of cell lines
- 250 stable CHO cell pools for screening campaigns in 8 weeks

PROVEN
- More than 20 Selexis generated cell lines are in clinical trials up Phase 3
- Technology has been and is currently being used by more than 50 companies worldwide

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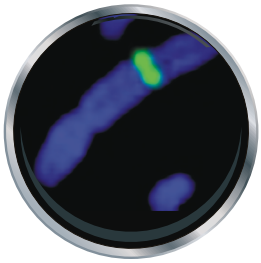
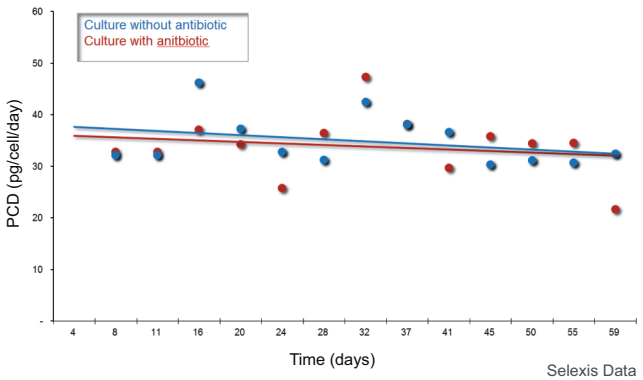
Selexis CHO-M Cell Line Stability



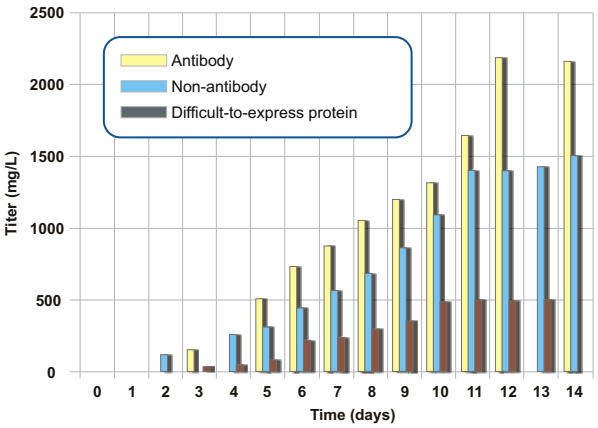
- ✓ Integration at single and unique site
- ✓ No chromosomal rearrangements/ aberration
- ✓ Very stable integration position sites

Stability of Selexis CHO-M Expressing IgG_1



Selexis Data

Case Study: From DNA to IND in 14 Months



Varghese J, Alves W, Brill BJ, Wallace M, Calabrese D, Regamey A, Girod P. Rapid Development of High-Performance Stable Mammalian Cell Lines for Improved Clinical Development. *BioProcess J*, 2008; 7(4): 30-36.

MERRIMACK PHARMACEUTICALS

- From DNA to IND in 14 months
- **ANTIBODY**
  >2 grams per liter
- **NON-ANTIBODY PROTEINS**
  >1g per liter
- **DIFFICULT-TO-EXPRESS PROTEIN**
  .5g per liter

Clients' Pipeline Using SURE*technology*™

THERAPEUTIC CANDIDATES	Discovery/ Pre-clinical	Phase 1	Phase 2	Phase 3	Market
Oncology	9	8	2		
Inflammation	7	9		1	
Blood disorders	5			2	
Asthma, allergies, respiratory	4	2			
Dermatology		1			
R&D Licenses	17				

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