Development of stable CHO cell lines

Establishment of time-and cost-efficient processes to identify high producer clones with a minimal screening effort

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Since more than 20 years, InVivo is dedicated to the development and production of high quality monoclonal antibodies (mAB) and recombinant proteins. Moreover, we generate stable non-GMP CHO cell lines to produce high yields of antibodies and proteins for preclinical studies.

Production of biopharmaceuticals is very costly and requires a high degree of forward planning. The production capacity in GMP facilities is often limited and therefore production slots need to be reserved well in advance. In many cases, the characterization of potential new drug candidates is still ongoing at this stage of development and it´s hard to predict the success of distinct targets.
However, to speed up the research and development process and to limit unnecessary costs, a large part of pre-clinical studies can be carried out using stable non-GMP cell lines.

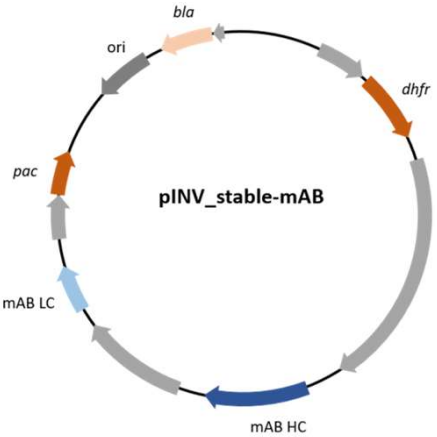
Maximizing mAB yield by using the right set of tools

CHO suspension cells as suitable host for biopharmaceutical production

CHO cells are the most common cell type in production of biologics and biosimilars.
Throughout years, we optimized the well-established cell line CHO-IS and adapted it to our high-performance chemically-defined, animal component-free medium. The cells are extremely robust, productive and qualified for large scale application. The development of high-cell-density processes in standard bioreactors enables cost-optimized production of large quantities of target proteins.

Optimizing mAB expression through a novel vector set for stable transfection of CHO cells

We developed a set of novel expression vectors that are compatible to the PiggyBac system for the efficient generation of stable CHO cell lines:
These include an one-promotor plasmid for the stable expression of recombinant proteins, a two-promotor plasmid for the efficient expression of antibodies, and a helper plasmid for providing the transposase to the cells.



bla = gene encoding ß-lactamase; mediates prokaryotic resistance against ampicillin. ***pac*** = gene coding for puromycin *N*-acetyltransferase; mediates resistance against puromycin. ***dhfr*** = gene encoding dihydrofolate reductase; mediates resistance against folic acid analogues like methotrexate. Light grey arrows = promotor regions.

Workflow

PEI-mediated transfection

Double selection of stable expressors with puromycin and MTX

Selection of the best producing pool

Selection of high producing monoclones. Monoclonality is documented via NyOne

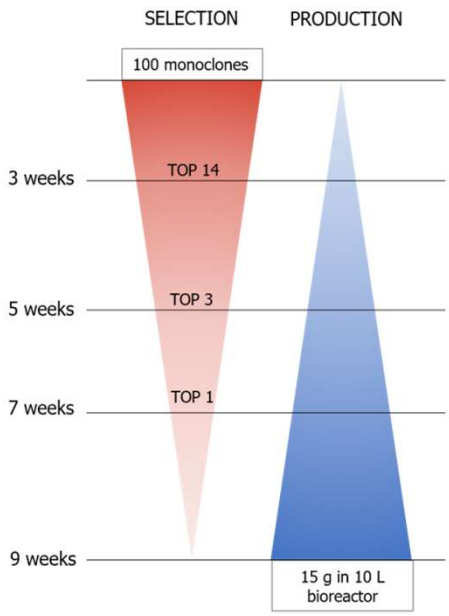
Production (I): Fed-Batch Shaker Assay (3L)

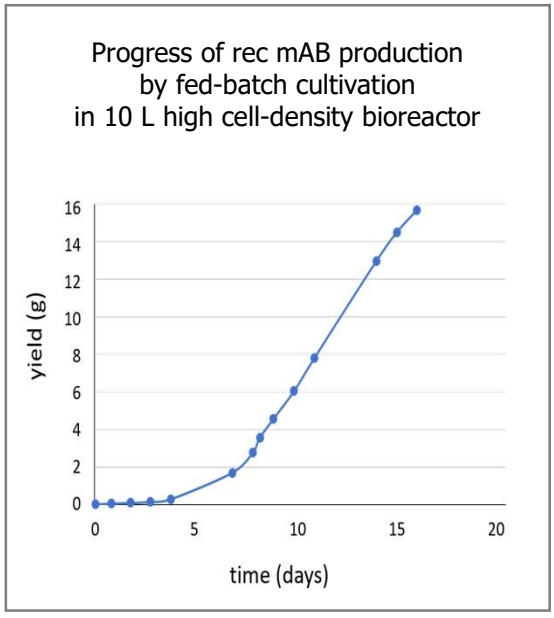
Production (II): Fed-Batch fermentation in 10L bioreactor

Protein purification and quality control

Through years of optimization work, InVivo successfully established a highly-efficient process for the generation of stable CHO cell lines for research and preclinical use.

We reduced the costly and labor-intensive screening work and simultaneously improved the selection process and enhanced the productivity of the selected monoclones.
This was possible by combining a novel set of expression vectors with our high-quality serum-free medium and a sophisticated high cell-density fed-batch fermentation process.
Now, we are able to identify clones producing a final yield of around **15 g** of **antibody**, in a 10 L bioreactor run, while only screening a limited set of **100 monoclones**.





Advantages of InVivo stable cell line development services:

✓ **FAST:**	Short timeline through effective screening approaches and optimized high-yield antibody production
✓ **INEXPENSIVE:**	Cost-efficient production through implemented equipment and well-defined processes
✓ **NOW:**	No long waiting times for production slots – we can start the development of your CHO cell line right away