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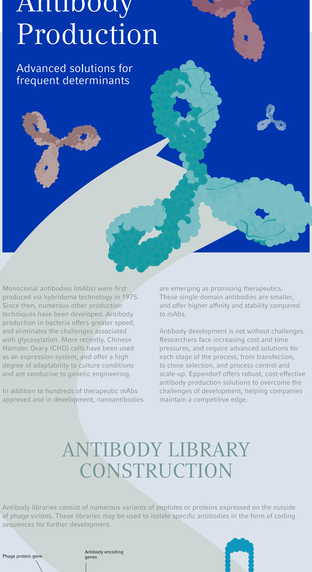
Antibody Production

Advanced solutions for frequent determinants



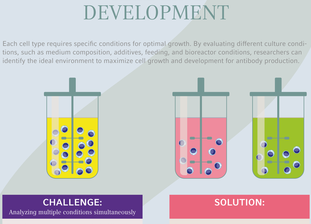
Monoclonal antibodies (mAbs) were first produced via hybridoma technology in 1975. Since then, numerous other production techniques have been developed. Antibody production in bacteria offers greater speed, and eliminates the challenges associated with glycosylation. More recently, Chinese Hamster Ovary (CHO) cells have been used as an expression system, and offer a high degree of adaptability to culture conditions and are conducive to genetic engineering.

In addition to hundreds of therapeutic mAbs approved and in development, nanoantibodies are emerging as promising therapeutics. These single-domain antibodies are smaller, and offer higher affinity and stability compared to mAbs.

Antibody development is not without challenges. Researchers face increasing cost and time pressures, and require advanced solutions for each stage of the process, from transfection, to clone selection, and process control and scale-up. Eppendorf offers robust, cost-effective antibody production solutions to overcome the challenges of development, helping companies maintain a competitive edge.

ANTIBODY LIBRARY CONSTRUCTION

Antibody libraries consist of numerous variants of peptides or proteins expressed on the outside of phage virions. These libraries may be used to isolate specific antibodies in the form of coding sequences for further development.



CHALLENGE:
PCR Bottlenecks

Polymerase chain reaction (PCR) is used for amplifying specific coding sequences in RNA isolated from mammalian cells prior to ligation into the phage display vector. Long runtimes create bottlenecks and reduce productivity.

SOLUTION:

Fast ramping thermal cyclers can accelerate heating and cooling cycles, reducing total runtime. A ramp rate of 10°C/s can reduce runtime to under 40 minutes.

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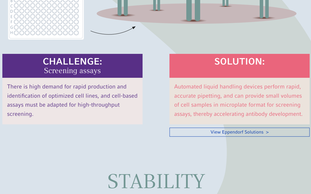
CELL LINE DEVELOPMENT

Each cell type requires specific conditions for optimal growth. By evaluating different culture conditions, such as medium composition, additives, feeding, and bioreactor conditions, researchers can identify the ideal environment to maximize cell growth and development for antibody production.



CHALLENGE:
Analyzing multiple conditions simultaneously

It may be necessary to assess multiple different experimental conditions to identify the conditions that support optimal growth. Running sequential experiments is time-consuming and inefficient.

SOLUTION:

A parallel mini bioreactor system enables monitoring of up to 16 or 24 different bioreactors simultaneously, and is an efficient approach for determining optimal conditions.

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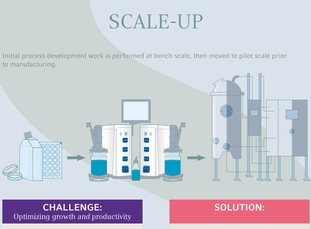
CELL LINE SELECTION

After being transfected with plasmids expressing selectable markers, cell lines must be screened to identify productive, stable clones. Enzyme-linked immunosorbent assays (ELISAs) are often used as a primary screen, followed by additional assays to determine growth and productivity of clones expressing specific markers.



CHALLENGE:
Screening assays

There is high demand for rapid production and identification of optimized cell lines, and cell-based assays must be adapted for high-throughput screening.

SOLUTION:

Automated liquid handling devices perform rapid, accurate pipetting, and can provide small volumes of cell samples in microplate format for screening assays, thereby accelerating antibody development.

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STABILITY

Antibody stability is essential for expression, activity, specificity and even storage.

CHALLENGE:
Preventing degradation

Antibodies may degrade when exposed to various stressors, such as high and low pH, freeze-thaw cycles, and mechanical stresses like agitation. Identifying these stressors early can provide valuable insights into manufacturability.

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SOLUTION:

Forced degradation studies are designed to expose antibody products to various stressors. For example, ultra-low temperature freezers may be used to perform multiple cycles of freezing to -80°C, and shaking at 200 rpm or higher may be use to stimulate aggregate formation.

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SCALE-UP

Initial process development work is performed at bench scale, then moved to pilot scale prior to manufacturing.

CHALLENGE:
Optimizing growth and productivity

It is important that cells grow well during scale-up, but different bioreactor conditions may be required to optimize antibody production.

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SOLUTION:

Parallel bioreactors may be used to assess two different mediums, one designed to optimize cell growth, the other to optimize antibody production.

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EMERGING TECHNOLOGY

Nanoantibodies are therapeutic proteins consisting of single-domain antibody fragments derived from naturally occurring heavy-chain-only antibodies in the serum of camelids. Compared to mAbs, their smaller size, higher stability, affinity, and solubility make them attractive candidates for therapeutic development. Numerous nanoantibodies are under clinical investigation as treatment for cancer and infectious diseases, among others. Nanoantibodies may be produced from heavy-chain antibodies, conventional antibodies, or human single-domain antibodies.

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To learn more, visit:
www.eppendorf.com/antibodies

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*This infographic was created in cooperation with Lab Manager