Chinese Hamster Ovary-K1 Cells

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CHO cells are epithelial-like cells isolated from Chinese hamster ovary. The original CHO cells are cultured adherently, but they can be cultured in suspension in serum-free medium after acclimation. CHO cells are widely used for the expression of recombinant proteins.

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Chinese hamster ovary (CHO) cells are the most important host system used for monoclonal antibody (mAb) expression. CHO cells were first isolated by the Puck laboratory in 1957 and obtained by enzymatic digestion of Chinese hamster ovary tissue. In 1958, the Puke laboratory re-cloned the serially passaged cells and established the most primitive cell line of CHO cells we are currently using. The most primitive CHO cell line is proline-deficient, and extra proline must be added to the medium to support its growth. All currently known CHO cell lines retain this characteristic. This most primitive CHO cell line was later transferred to different laboratories and companies, and different types of CHO cell lines were formed after different cultivation, domestication, transformation and recloning. Although these cell lines are derived from the most primitive CHO cell lines, due to the inherent instability of the CHO cell genome and the subsequent selection and culture conditions of different laboratories, the morphology, growth, expression, and metabolism of different CHO cell lines , and even genomes are quite different. The following describes several commonly used CHO cell lines.

1) CHO-K1; CHO-K1 is an unmodified wild-type CHO cell. The original CHO-K1 was deposited in ATCC (CCL-61) and named a subclone of the original CHO cell line by Puck and Kao's laboratories around 1970. Subsequently, a subclone derived from ATCC CHO-K1 was isolated in 1985 and stored in ECACC (85051005), and was used by pharmaceutical companies and CMO companies to express recombinant proteins. The most primitive CHO-K1 cells are adherent culture, and need to add serum. After Lonza obtained CHO-K1 from ECACC and acclimatized it to suspension serum-free culture, established the CHO K1SV (Lonza, 2002) cell line, which was widely used in its GS expression platform. Merck (formerly SAFC) also obtained the CHO-K1 cell line from ECACC, and was suspended and acclimated in a chemically limited medium to form the CHOZN® CHO K1 (Merck, 2006) cell line. CHO-K1 cell-based expression platforms mostly use GS (glutamine synthetase) screening system and/or antibiotic screening system. Two screening systems are used in conjunction to improve screening efficiency. At present, many therapeutic proteins that have been marketed are developed and produced based on CHO-K1 cells.

2) CHO-S: based on the original CHO cell line, Thompson's laboratory isolated a CHO cell that can be used for suspension culture in 1973 and named this cell CHO-S. This cell line was provided to the Gibco company in the late 1980s, which domesticated the cell into CD CHO medium, built a bank and promoted it under the name of CHO-S. Because it can grow in suspension in a serum-free medium and supports high-density culture, it is often used as a transient expression host cell in the early stage. Since then, the corresponding GMP cell bank was established and supported the development of commercial authorization.

3) CHO-DXB11: CHO-DXB11 (also known as DUK-XB11) was obtained by Urlaub and Chasin of Columbia University through gamma-ray mutagenesis in the 1970s and 1980s. Among the biallelic genes of CHO-DXB11 cells, one DHFR gene was knocked out, and the other DHFR gene contained only a missense mutation (T137R), which prevented the cell from effectively reducing folate and synthesizing hypoxanthine (H) and thorax. Glycoside (T). When expressing exogenous recombinant protein, the exogenous DHFR gene and the target protein gene are transfected into the cells at the same time, and the cells are screened through a medium lacking HT.
The first recombinant protein approved for marketing on the CHO cell platform uses DXB11 as the host cell, and this host cell is used by Genentech for the subsequent production of multiple commercial products.

4) CHO-DG44: since only one allele in DXB11 cells has been knocked out, during the long-term passage process, there will be a low probability of mutations that will restore the activity of the DHFR gene in the host cell, resulting in a decrease in screening pressure and even a decrease in recombinant protein expression. Therefore, it has become a requirement to obtain a host cell in which the biallelic DHFR gene is completely knocked out. Through chemical mutagenesis and

gamma-ray mutagenesis, Chasin laboratory finally screened out the CHO host cell with biallelic DHFR gene knockout in 1983, and named it CHO-DG44. Because DG44 cells completely lack the activity of the DHFR gene and can be cultured in serum-free suspension, the screening and pressurization process becomes more effective. At present, many companies and CDMO companies use this cell as a platform for the development of therapeutic proteins, and many products have entered the clinical and marketing stage

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