GENOTYPE OF CHO HOST CELL LINE HAS HIGHER IMPACT ON MAB PRODUCTION AND QUALITY THAN PROCESS STRATEGY OR CELL CULTURE MEDIUM

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Chinese hamster ovary (CHO) cells comprise a variety of lineages, including CHO-DXB11, CHO-K1, CHO-DG44 and CHO-S. Despite the fact that CHO cell lines share a common ancestor, extensive mutagenesis and clonal selection have resulted in substantial genetic heterogeneity among them. Data from sequencing shows that different genes are lacking from individual CHO cell lines and that each cell line harbors a unique set of mutations that are relevant to the bioprocess. However, literature outlining how the observed genetic differences affect CHO cell performance during bioprocess operations remains scarce.

In this study, we examined host cell-specific differences among three widely used CHO cell lines (CHO-K1, CHO-S and CHO-DG44) and recombinantly expressed the same monoclonal antibody (mAb) in an isogenic format in all cell lines by using bacterial artificial chromosomes (BACs) as transfer vector. Cell-specific growth, product formation and heavy and light chain mRNA levels were studied in batch, fed-batch and perfusion cultures. Furthermore, two different cell culture media were investigated.
Product quality was studied through glycoprofiling, and the thermal denaturation was analyzed using differential scanning calorimetry (DSC).

We found CHO cell line-specific preferences for mAb production or biomass synthesis that were determined by the host cell line rather than product-specific mRNA levels. Additionally, quality attributes of the expressed mAb were influenced by the host cell line and medium used.