POPULATION DYNAMICS IN CLONED CHO CELL LINES

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The inherent nature of cloned CHO cell lines includes the presence of genetic and phenotypic drift that leads to heterogeneous populations. The genetic heterogeneity exhibited by these cells can be exploited to understand the population dynamics of cloned cell lines. One way to track heterogeneity within populations is by utilizing genetic sequence variants (SVs) as biomarkers for distinct populations. In the experiments described here, cell lines with varying levels of sequence variants resulting from a single nucleotide change in the gene of interest were used to study population dynamics in cloned CHO cell lines.

Analysis of four different monoclonal antibody-expressing cell lines with known sequence variants under varying continuous culture conditions provided insight into transcription and translation rates of SV-containing cell lines and allowed us to generate population dynamic models leading to better understanding of SVs and the genetic heterogeneity of clonal cell lines. Early time points of these cell lines were further subcloned and analyzed to gain further understanding of subpopulation dynamics in cloned cell lines and the results of these experiments will be presented. Subclones of these four clonal cell lines proved varying degrees of heterogeneity while falling into distinct population dynamics models.

Additionally, mixing of subclones expressing the same mAb, with and without SVs at similar growth rates allowed us to evaluate how populations shift over time. A range of expected and unexpected outcomes was observed with these intentionally mixed populations demonstrating the complexity of clonal cell line heterogeneity. This study will further our understanding on the interplay between clonality, heterogeneity and population dynamics of “clonal” cell lines and will allow for critical assessment of overarching cell line development methods and strategies.