ADVANCED CELL CULTURE PERFORMANCE BY RATIONAL MEDIA DESIGN BASED ON IN DEPTH PROCESS UNDERSTANDING

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Monoclonal antibodies are the leading class of biopharmaceuticals. These products are mainly produced in processes with CHO cells. A robust cell culture media platform becomes key to develop an efficient and robust production process. A comprehensive screening was performed to detect substances with the potential to improve the cell culture performance without impacting the media stability. Nineteen substances with potential effects on cysteine metabolism, cell cycle, reactive oxygen scavenger, histone deacetylase inhibitor or intracellular cAMP were spiked to the standard fed-batch process in different concentrations. Especially substances impacting the cysteine metabolism showed the ability to prolong specific productivity and viability during the last days of the fed-batch process. The intracellular data revealed a metabolic understanding of the connection between cysteine concentration and detox pathways (Figure 1).

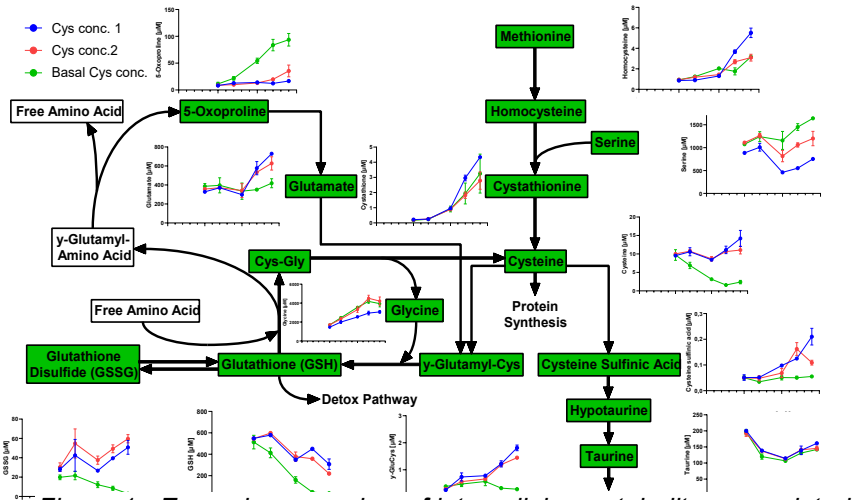
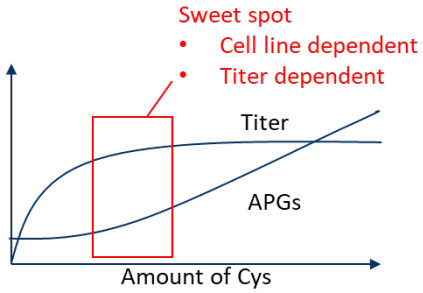


Figure 1 - Exemplary overview of intracellular metabolites associated with Cys metabolism when feeding different amounts of Cys.



Additional optimization experiments focusing on the cysteine metabolism showed a sweet spot with an increased process performance (viability and titer) without negatively affecting PQ and media stability (Figure 2).

Figure 2 - Cys sweet spot to ensure titer optimum without affecting PQ.

Among the high number of media components, cysteine is of particular interest as it plays a pivotal role in achieving prolonged cell viability and high product concentrations. Furthermore, it also has a high impact on PQ, media reactivity and stability.