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MONITORING INTRACELLULAR COMPONENT POOLS TO IDENTIFY STEADY STATE IN MAMMALIAN CELL PERFUSION CULTURE

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Key Words: mammalian cells, perfusion culture, steady state, MALDI-TOF MS, intracellular components

Perfusion cultures of mammalian cells are a well-considered alternative in the process development for new biologic products. Stable operation of the culture should eventually lead to a steady state, positively effecting product quality. Although macroscopic variables such as viable cell density, main metabolite or product concentrations are observed constant, little is known about the extent of steady state on intracellular level.

In this study intracellular component pools of CHO cells were monitored at different steady states in perfusion cultures using matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS). A novel single extraction was used to separate metabolite, lipid as well as protein fractions and quantify their constitution according to associated internal standards. Statistical tools were applied to resolve characteristic steady state attributes

This approach allowed a comprehensive insight on metabolic as well as protein expression level. Identified features were used to explain differences between the examined states. Gained knowledge can be applied in further process optimization.