

HIGH-THROUGHPUT APPLICATION OF METABOLIC FLUX ANALYSIS FOR INVESTIGATION OF MAMMALIAN CELL CULTURE PERFORMANCE

Christine Davis, Shire HGT, Inc, Lexington, MA, a member of the Takeda group of companies
christine.davis@takeda.com

Jacqueline Gonzalez, Shire HGT, Inc, Lexington, MA, a member of the Takeda group of companies

Key Words: metabolic flux analysis, AMBR15, high-throughput

An important consideration in bringing a new molecule through development is speed to clinic. Increased utilization of high throughput tools, process platforms, and *in silico* modelling can allow for screening of more conditions in a shorter period of time, enabling either a faster development time or increased optimization capability.

Here we discuss the application of a basic metabolic flux analysis model to better understand and manipulate mammalian cell culture performance. With this tool, we aim to improve hypothesis-generation and design experiments more rationally. Studies were performed across multiple CHO cell lines producing various recombinant enzyme products in both 10L benchtop bioreactors and an AMBR15 small-scale system. Based on predictions from the metabolic flux analysis model, certain amino acids were supplemented in the media to modulate growth rate, titer, and metabolic byproducts. Effects on these parameters were then assessed and compared across process scales and cell lines.

This case study demonstrates the utility of high throughput process development tools in conjunction with metabolic modelling for better understanding of existing processes and cell lines. This method of screening provides the comprehensive data sets that are necessary to elucidate effects of amino acid supplementation on mammalian cell culture performance. Additionally, application of *in silico* modelling techniques such as this may lead to fewer required experiments, shortening development timelines.