

## APPLICATION OF -OMICS KNOWLEDGE YIELDS ENHANCED BIOPROCESS PERFORMANCE

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The classic phrase to describe cell culture is “every cell line is different.” The unfortunate part of this idiom is the actual concealment of a crucial lack of fundamental understanding. Furthermore the phrase ignores the substantial success achieved to date in developing robust industrial cell culture platforms that are applied to all cell lines regardless of their intrinsic variation. At Biogen, our cell culture medium platform is agnostic to CHO host cell line, and the platform can accommodate this inherent genomic variation as cell lines come from different host backgrounds. This is also an opportunity for -omics work then as the differences in cell line performance can be linked back to fundamental differences within those host cell lines. However, the power of -omics technologies to influence process optimization is limited by the difficulty and time scale for execution and interpreting such studies.

Our approach to -omics implementation has been to utilize multiple targeted investigations and combine the learnings into an implementation strategy focused on enhancing the efficiency of manufacturing. Metabolic flux analysis was used to establish a baseline knowledge of central metabolism in the Biogen platform. The next step was to incorporate transcriptomics and proteomics with our metabolomics knowledge. With Biogen’s toolbox of CHO host cell lines, this approach identified intrinsic host cell line differences as well as unique limitations in cell culture. Specifically, we have determined sources of novel metabolic inhibitors that suppress cell growth as well as differences in lactate and ammonium metabolism that split according to host cell source. These conclusions ultimately lead to the optimized platform process yielding the desired product quality. Determining these differences led to an increased growth rate in scale up for cell lines from a more sensitive host as well as maintaining robust cell growth and productivity in production bioreactors. Ultimately still “every cell line is different.” Yet the more we know, the more opportunities there are to exploit both the similarities and the differences.