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## ENHANCING SITE-SPECIFIC CHO PRODUCED ANTIBODY THROUGH MEDIA OPTIMIZATION USING METABOLOMICS APPROACH

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Chinese hamster ovary (CHO) cells have been widely used to produce recombinant protein. Several serum-free and chemically defined CHO medium are available for industrial manufacturing of recombinant antibodies. However, the effect on the cell metabolism and antibody productivity with different chemically defined basal media and feeds is still unclear. Recently, metabolic engineering become a powerful approach for medium optimization. In this study, we performed metabolic profiling (amino acids) by UPLC and compared two different commercial chemically defined basal media in batch and basal media with feeds in fed-batch culture system. We also compared the antibody productivity of site-specific high producing cell lines with chemically defined media. In batch culture, the highest cell concentrations and antibody titer was similar in two chemically defined CHO medium or mixed medium. However, in fed-batch culture, the highest cell concentrations ( $36 \times 10^6/\text{ml}$ ) were obtained in mixed medium with optimized feeds. The antibody titer of fed-batch in mixed medium with feeds was significantly higher than that of batch culture (up to 14 fold). Through the application of metabolite and pathway analysis, the fed-batch media can be further optimized.