HIGH-YIELD ANTIBODY PRODUCTION USING TARGETED INTEGRATION AND EMGINEERED CHO HOST

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To identify the high expression sites in the CHO cells, we employed NGS to analyze the integration sites of a high producing cell line (titer > 3g/L). The pair-end reads with one read mapped to the vector and the other read mapped to the CHO reference genome are extracted to identify the integration sites. To test the expression activity of the integration sites, we employed CRISPR/Cas9 to specifically integrate the antibody gene into CHO genome for expression. Our data showed 4 integration sites are in the high producing cell line. Among the 4 integration site, one integration site was tested by CRISPR/Cas9 for target integration of antibody gene for expression. The target integrated cell pool present higher expression level (130 mg/L/copy) and less copy number when compared other integration sites. Through single-copy integration method, we can also achieve 60-150 mg/L/copy in a batch culture. About 80% of the single-copy cell clones were stable at generation 60. We have also applied the CHO-specific microarray transcriptomics technology to identify genes that contribute to high productivity. Transfection of our proprietary dual promoter vector J 1.0 resulting in 1.65 to 2.4 fold increase in the expression in engineered CHO DXB11 host. Through fed-batch process development, 3 – 5 g/L mAb productivity can be achieved through targeted integration and engineered CHO host.