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Generation of desirable CHO cell factories with predictive culture performance using CRISPR/Cas9-mediated genome engineering

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Chinese hamster ovary (CHO) cells are widely used in the biopharmaceutical industry as a host for the production of complex pharmaceutical proteins. Thus, genome engineering of CHO cells for improved product quality and yield is of great interest. Here, I will demonstrate our latest advances in improving the efficiency of CRISPR/Cas9-mediated genome engineering to generate attractive knockout and knockin CHO cell lines. Analysis of the dynamics and efficiency of the technology will be demonstrated for genes involved in glycosylation and apoptosis. Combined with multiplexing and fluorescent enrichment, application of CRISPR/Cas9 genome editing facilitated disruption of several genes simultaneously and accelerated analysis of gene combinations. Engineered CHO cell lines with multiple disruptions of genes involved in apoptosis and glycosylation showed prolonged growth and improved glycosylation profiles. Site-specific integration of transgenes mediated by CRISPR/Cas9 and homology directed repair facilitated generation of targeted integrants with improved clonal homogeneity compared to random integrants. Improvements in the efficiency of our targeted integration platform combined with identification of good integration sites has facilitated precise insertion and expression of genes encoding biopharmaceuticals. In the end, characterization of engineered CHO cell lines with desirable properties generated using combinations of gene disruptions and insertions will be presented. The proven efficacy of genome engineering mediated by CRISPR/Cas9 technology has a large potential to accelerate current CHO engineering efforts. Together with high-throughput technologies, computational models and systems biology approaches, genome editing can pave the way for accelerated generation of desirable CHO cell factories with predictive culture performance.