HOST CELL PROTEIN CONTROL VIA CHO GENOME ENGINEERING

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Chinese hamster ovary (CHO) cells, a major mammalian platform in biomanufacturing, produce and secret recombinant proteins along with host cell proteins (HCPs). Because residual HCPs in the final drug product can adversely affect (1) patients by causing immune responses, (2) drug efficacy, and (3) product stability, the effective removal of HCPs is necessary. Unfortunately, many studies have reported that many HCPs can be difficult to remove through downstream purification processes because they share similar biophysical properties to biopharmaceuticals. In this study we employed a genome engineering approach using clustered regularly interspaced short palindromic repeats and associated protein 9 (CRISPR/Cas9) system-mediated knockout to address difficult-to-remove HCP problems. Three HCPs (Cathepsin D, Nidogen-1, and Prosaposin) that are known to be difficult to remove were selected, and respective knockout clones were isolated without using selective reagents or reporter genes. Clones for each HCP were characterized using various analysis methods. Taken together, we demonstrate the applicability of the CRISPR/Cas9 system to eliminate difficult-to-remove HCP expression in an industry-relevant setting.