A Chinese Hamster Ovary Cell Host Cell Protein That Impacts PS-80 Degradation

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The recent sequencing of the Chinese hamster and Chinese hamster ovary (CHO) cell genomes enables cell engineering strategies to address a wide variety of problems encountered in biopharmaceutical manufacturing. One particular application involves studies of CHO host cell proteins (HCPs) that may be difficult to remove for a variety of reasons. The presence of HCPs is regulated for patient safety concerns but may also have an impact on product quality in the context of formulation. Polysorbates are a class of non-ionic surfactants that are added to biopharmaceutical formulations to improve the stability of therapeutic proteins by limiting aggregation and surface adsorption. Monoclonal antibody formulations often incorporate polysorbate 80 (PS-80) to prolong the shelf-life of drug products. PS-80 degradation over time can impact the stability of those drug products.

We studied a range of CHO HCPs that are difficult to remove for a variety of reasons including HCPs that coelute with various monoclonal antibodies, HCPs that may bind to various monoclonal antibodies, and HCPs that change in expression as a function of cell age. We identified one HCP, HCP A, that is particularly difficult to remove. Based on the function of this protein, we hypothesized that the presence of this molecule in PS-80 containing drug formulations may result in increased degradation rates of PS-80. We used an interfering RNA approach to reduce the expression of HCP A in CHO cells. Those modified cells exhibited a significantly lower level of expression of HCP A than control cells, as measured by a mass spectrometry-based assay that was developed to quantify HCP A expression, without significantly impacting cell viability or cell density. The HCP from cells modified with the interfering RNA exhibited substantially reduced hydrolysis of PS-80 relative to HCP derived from control cells. Additional observations based on genome editing strategies to knock out the HCP A gene will be discussed.