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A multi-omic approach to understanding recombinant protein degradation in Chinese hamster ovary cells

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Product degradation, such as proteolytic clipping, is a common quality issue with the recombinant expression of proteins from Chinese hamster ovary cells in the biopharmaceutical industry. In this study we applied a “multi-omic” approach including RNA-seq, miRNA and proteomic analysis to identify factors contributing to the degradation of a model recombinant molecule. We identified 19 recombinant Chinese hamster ovary clonally-derived cell lines producing various levels of truncated or clipped product from a fed-batch cell culture shake flask screen. These cell lines then underwent detailed analysis using the various ‘omic approaches to identify the key causal factors linked to truncation of the recombinant molecule. Bioinformatics analysis of both the transcriptomic and proteomic data identified a number of candidate proteins (including proteases) that are likely to play a role in the truncation of the molecule. Targeted functional assays involving siRNA knockdown and inhibitor approaches were applied to reduce degradation of the protein.