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National Institute for Bioprocessing Research and Training

Contract Research

CASE STUDY

Post-Translational Modification (PTM) identification and monitoring of biotherapeutic stability samples

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Challenge

A client requested the support of NIBRT Contract Research to identify post-translational modifications (PTMs) in stability samples. The client was developing a new format for their biotherapeutic and had observed changes in the charge variant profile of the stability samples with their lead formulation. An in-depth characterization of the PTMs would allow the client to identify the attributes that were contributing to the change in charge profile. As part of the study two alternative formulations were also analysed in order to assess the optimal formulation.

Solution

Samples of the different formulations were provided from several stability time points to allow monitoring of PTMs. A peptide mapping approach was employed to identify PTMs and compare abundance across samples. Following trypsin digestion tryptic peptides were separated and analysed by RP-LC-MS/MS. The resultant mass spectrometric raw data was analysed using the PTM workflow in the Byos® software package from Protein Metrics for identifying post-translational modifications (PTMs). The data was manually interrogated to exclude false positives by observing the MS1 and MS2 data leveraging on the experience of the subject matter expert (SME) analyst. PTMs were quantified within the Byos® software as the XIC (extracted ion chromatogram) ratio of the modified peptide form relative to the wildtype form.

Outcome

A comprehensive report was provided to the client reporting all identified PTMs for all samples. A variety of PTMs were identified and the client was able to make conclusions on which modifications could be attributed to the change on charge variant profile. Data from this analysis enabled the client to select the optimal formulation by comparing the three formulations analysed.

Project Process

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