NEWS:

Have a wonderful 2022 year with Phylogene

If you missed out our January month posts on Linked In, now the time to catch-up! Post were addressing Host cell proteins detection and removal in bioproduction.

Host Cells Proteins analysis: Now the time for LC-MS/MS

Host Cells Proteins (HCPs) are byproduct inherent to drug production processes, generated by the producing organisms (e.g. E.coli, CHO and HEK cells …). Due to their harmful immunogenicity potential, HCPs should be removed during several purification steps until final drug substance production. HCP's induced risks have to be carefully assessed and HCPs' presence carefully evaluated during the development process ''cf: ICH guidance Q6B (1999)''.

For years, HCP total content has been assessed using ELISA methods, however its limited outcome answered partially and most of the time incompletely to regulatory and industry needs ; additional orthogonal methods being necessary to complete and finalize the analysis. **LC-MS/MS** is able to provide additional details about the individual HCPs and their quantity without the long development and immunization process of a specific ELISA.

LC-MS/MS is the methodology allowing the fulfillment of your industrial requirements in only one experiment.

The future of host cell protein (HCP) identification during process development and manufacturing linked to a risk based management for their control

''The use of biological systems to synthesize complex therapeutic products has been a remarkable success. However, during product development, great attention must be devoted to defining acceptable levels of impurities that derive from that biological system, heading this list are host cell proteins (HCPs). Recent advances in proteomic analytics have shown how diverse this class of

impurities is; as such knowledge and capability grows inevitable questions have arisen about how thorough current approaches to measuring HCPs are''…'' These issues have led to the investigation of orthogonal analytical methods; most prominently mass spectrometry. These techniques can potentially both identify and quantify HCPs.''

Tracking Host Cell Proteins During Biopharmaceutical Manufacturing: Advanced Methodologies to Ensure High Product Quality

''Targeted quantitation of individual HCP species contributing to the overall signal is not possible by HCP ELISA. The quantitative values obtained by the HCP ELISA represent a cumulative parameter of all the immune-reactive HCPs present in a particular sample in relation to the HCP reference standard. Furthermore, polyclonal anti-HCP antibodies are present in different quantities and show diverse affinity and avidity, limiting the capability of the HCP ELISA to quantify all HCPs with the same sensitivity. This could potentially lead to an over- or underestimation of particular HCPs. As a consequence of an extreme underrepresentation or complete absence of specific antibodies against certain HCPs, the latter may not even be detected at all. To overcome this limitation, it is highly recommended to use orthogonal methods. Mass spectrometry provides a universal approach to identify and characterize HCPs without the need for critical reagents like HCP reference standard or antisera. The liquid chromatography tandem mass spectrometry (LC-MS/MS) technique is capable of addressing the complexity and dynamic range of HCP pools in bio-process samples, typically with a sensitivity in the lower ppm range, enabling detection of high to moderate abundant HCPs in purified drug substance material''

Challenges to industrial mAb bioprocessing - removal of host cell proteins in CHO cell bioprocesses

''The era of personalised medicine is upon us and with biopharmaceutical companies increasingly investing in R&D pertaining to the development of therapeutic monoclonal antibodies (mAbs) it is unsurprising that mAbs are at the forefront of the biopharmaceutical industry. Monoclonal antibodies hold a steadfast lead in the ever-expanding biologics marketplace and have revolutionized the treatment of a wide variety of illnesses. The prominence of mAbs as therapeutic agents brought with it the need for large scale production of these drugs, which in turn highlighted the need for improvements in cell culture processes to raise product titres. Increased product titres shifted bioprocessing concerns downstream as with increased titre brought along the increased expression of unwanted host cell proteins (HCPs). HCPs are a highly diverse range of proteins. While some HCPs can be degradative to the product itself, others could induce an unwanted immune response compromising the safety and efficacy of the biologic. Enzyme-linked immunosorbent assays (ELISAs) are currently the gold standard for release testing for HCPs. ELISAs provide quantitative measurement of total HCP levels but have several limitations. Industry has shifted towards the use of orthogonal methods to support process development and validation with a particular focus on analytical tools such as LC–MS/MS.''

Applications of proteomic methods for CHO host cell protein characterization in biopharmaceutical manufacturing

''While HCP ELISA remains a critical tool for bioprocess development, proteomic methods have significantly increased the understanding of HCP dynamics, including both production and removal. Proteomic analyses have enabled identification of the most problematic HCP impurities, including those that are immunogenic, difficult to purify, and degrade both product molecules and excipients. These studies have begun to show the links among upstream process conditions, downstream HCP clearance''

With Phylogene you can characterize HCPs during your drug biodevelopment process or your proteins bioproduction!

Just think out of the box!

1- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4973824/pdf/BIT-112-1727.pdf

2- https://www.americanpharmaceuticalreview.com/Featured-Articles/347250-Tracking-Host-Cell-Proteins-During-Biopharmaceutical-Manufacturing-Advanced-Methodologies-to-Ensure-High-Product-Quality/

3-https://www.sciencedirect.com/science/article/abs/pii/S221133981830039X

4-https://www.sciencedirect.com/science/article/abs/pii/S221133981830039X

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