Serum-abundant protein depletion

Serum-abundant protein depletion refers to the removal or reduction of highly abundant proteins from serum or plasma samples to facilitate the analysis of lower-abundance proteins. In biological samples such as blood, a few proteins are present in large quantities, making it difficult to detect and study less abundant proteins of interest. Removing or depleting these highly abundant proteins can help enhance the detection sensitivity and dynamic range of proteomic analysis methods.

The most commonly targeted abundant proteins for depletion include albumin, immunoglobulins (IgG), transferrin, haptoglobin, alpha-1-antitrypsin, and fibrinogen. These proteins can account for a significant portion of the total protein content in serum or plasma.

Several methods and commercial kits are available for serum-abundant protein depletion. These methods generally utilize affinity-based chromatography, immunodepletion, or a combination of both. Affinity-based chromatography involves using specific ligands or resins that bind to the abundant proteins, allowing for their selective removal from the sample. Immunodepletion utilizes antibodies that specifically bind to the targeted proteins, leading to their precipitation or removal.

After depletion, the remaining proteins in the sample, including the lower-abundance proteins, can be more easily analyzed using techniques such as mass spectrometry or protein assays. Depletion of abundant proteins can help identify and quantify proteins that might otherwise go undetected or be overshadowed by the presence of highly abundant proteins.

It's important to note that while abundant protein depletion can enhance the analysis of low-abundance proteins, it may also result in the loss or depletion of proteins of interest. Therefore, careful consideration and optimization of the depletion method are necessary to achieve the desired balance between abundant protein removal and preservation of the proteins of interest.

Ahsan et al. benchmarked five different serum abundant protein depletion (SAPD) kits with regard to the identification of disease-specific biomarkers in human serum using bottom-up proteomics. As expected, the IgG removal efficiency among the SAPD kits is highly variable, ranging from 70% to 93%. A pairwise comparison of database search results showed a 10%-19% variation in protein identification among the kits. Immunocapturing-based SAPD kits against IgG and albumin outperformed the others in the removal of these two abundant proteins. Conversely, non-antibody-based methods (i.e., kits using ion exchange resins) and kits leveraging a multi-antibody approach were proven to be less efficient in depleting IgG/albumin from samples but led to the highest number of identified peptides. Notably, the results indicate that different cancer biomarkers could be enriched up to 10% depending on the utilized SAPD kit compared with the undepleted sample. Additionally, functional analysis of the bottom-up proteomic results revealed that different SAPD kits enrich distinct disease- and pathway-specific protein sets. Overall, the study emphasizes that a careful selection of the appropriate commercial SAPD kit is crucial for the analysis of disease biomarkers in serum by shotgun proteomics 1).

1)

Ahsan N, Fornelli L, Najar FZ, Gamagedara S, Hossan MR, Rao RSP, Punyamurtula U, Bauer A, Yang Z, Foster SB, Kane MA. Proteomics evaluation of five economical commercial abundant protein depletion kits for enrichment of diseases-specific biomarkers from blood serum. Proteomics. 2023 May 18:e2300150. doi: 10.1002/pmic.202300150. Epub ahead of print. PMID: 37199141.