Abstract of Presentation

Plasma protein biomarker discovery and the PeptideAtlas

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Abstract :

The identification of protein biomarkers for the early detection and molecular definition of complex diseases such as cancer is a particular challenge in diagnosis and treatment. Human plasma proteome is an easily accessible, circulating representation of both physiological and pathological processes in tissues. Therefore, it is appealing to attempt to detect protein biomarkers in blood plasma. Unfortunately, direct comparisons of the blood proteomes of control and disease affected groups of individuals have not been very successful for the discovery of protein biomarkers. This is mainly due to the large complexity, high dynamic range and large person to person variability of plasma proteomes.

To overcome some of these limitations we have developed a new, hypothesis driven, targeted quantitative proteomic strategy for the discovery of plasma biomarkers. The strategy consists of three components. First, to overcome the large complexity of plasma proteins, we focus on glycosylated proteins. Since most proteins exposed by tissues to extracellular environments and secreted proteins are glycosylated we expect that the population of potential biomarkers is enriched for glycoproteins. Second, to avoid the necessity of measuring every plasma protein in every sample we are using comparative (tumor vs. healthy tissue) tissue glycoprotein analyses. The identified, differentially abundant glycoproteins are then quantified in plasma as a set of potential biomarkers. Third, the generated list of potential marker candidates is verified in plasma samples carrying out targeted analysis by multiple reaction monitoring (MRM) on glycopeptides isolated from the respective plasma samples. Precise absolute quantification is achieved by adding isotope labeled reference analytes. The inclusion of elution time constrains allows scheduling the MRM transitions and expanding the number of MRM measurements during one LC-MS run.

In the presentation we will discuss the strategy and illustrate its performance with selected examples.

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