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MS-based characterization of clinically relevant glycoproteoforms

Dynamically altering biomolecules are the true actors in studies on health and disease rather than genotypes or phenotypes that refer to a certain risk or an end-point observation. Unfortunately, clinically effective disease-specific tests that support diagnoses at an early and curable stage are still lacking for a wide variety of diseases. Proteoform-resolved data provides a layer of information additional to transcription, translation, and posttranslational events that underlie complex phenotypes. Of these, glycoproteoforms experience an increasing interest in providing personal baselines for diagnostic and disease monitoring purposes. It is hypothesized that determining a limited number of different species is sufficient to achieve clinical relevance and provide new means of patient stratification. In glyco-analytical strategies, mass spectrometry (MS) combined with different types of chromatography has dominated innovations, and glycoproteins such as transferrin and immunoglobulins are commonly identified and glyco-profiled in an intact or semi-intact manner [MCP 22(6) 100565 (2023)]. Top-down approaches are feasible, albeit that such methods report relative quantifications. As a rule, clinical implementation however requires precise characterization and quantification of glycoproteoforms with complementary strategies, namely released glycan- and glycopeptide-centric analysis, such as for antithrombin and prostate-specific antigen. It is foreseen that glycoproteoform analysis will provide unique phenotypes for each individual that combined with pattern recognition tools exhibit great potential in guaranteeing safe and accurate test results for patients in the era of precision medicine.

User consent

yes

Author: VAN DER BURGT, Yuri (Leiden University Medical Center)

Co-authors: Dr DOMÍNGUEZ-VEGA, Elena (Leiden University Medical Center); Prof. WUHRER, Manfred (Leiden University Medical Center)

Presenter: VAN DER BURGT, Yuri (Leiden University Medical Center)

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