Structural characterization of immunoglobulin G epitope (N-glycans) by MS-IR

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Mass spectrometry (MS) has become an essential part of the glycomics toolbox, allowing for instance to characterize N-glycans cores. N-glycosylation is a post-translational modification which may be involved in many diseases including rheumatoid arthritis (RA). However, MS is insufficient to describe entirely the terminal sugars of N-glycans (known as epitopes). Epitopes are not well understood because they present many isomers and they may carry diverse functional modifications introducing a lot of heterogeneity.

To characterize epitopes, we propose an original approach based on the coupling of tandem MS and infrared ion spectroscopy: InfraRed Multiple Photon Dissociation spectroscopy[1]. A mass spectrometer was modified to introduce a tunable IR laser inside the ion trap allowing to obtain simultaneously a mass spectrum and an IR fingerprint. These fingerprints will be helpful to characterize the isomerization of the compound.

Considering the importance of sialylated extremities in RA, we currently focused our research on this epitope present on immunoglobulin G. In this case, sialylated extremities will be present in two forms: sialic acid will be linked to a galactose via an α2.3 or an α2.6 linkage. Our strategy allows to determine their ratio. They can also present a rare modification: an O-acetylated group. Preliminary data on the position of O-acetylated groups are promising because regioisomers show distinctive IR fingerprints. Therefore, our approach could be a helpful tool for an early diagnostic of RA, using these rare glycome anomalies as biomarkers.

Bibliographic references:

(1) Schindler, B.; Barnes, L.; Renois, G.; Gray, C.; Chambert, S.; Fort, S.; Flitsch, S.; Loison, C.; Allouche, A.-R.; Compagnon, I. Anomeric Memory of the Glycosidic Bond upon Fragmentation and Its Consequences for Carbohydrate Sequencing. Nat Commun 2017, 8 (1), 973. https://doi.org/10.1038/s41467-017-01179-y.