

## Technology Offer

### Novel method for analysis of complex carbohydrate structures by ion-mobility mass spectrometry (IM-MS)

Ref.-Nr.: 0401-5070-MG

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#### Background

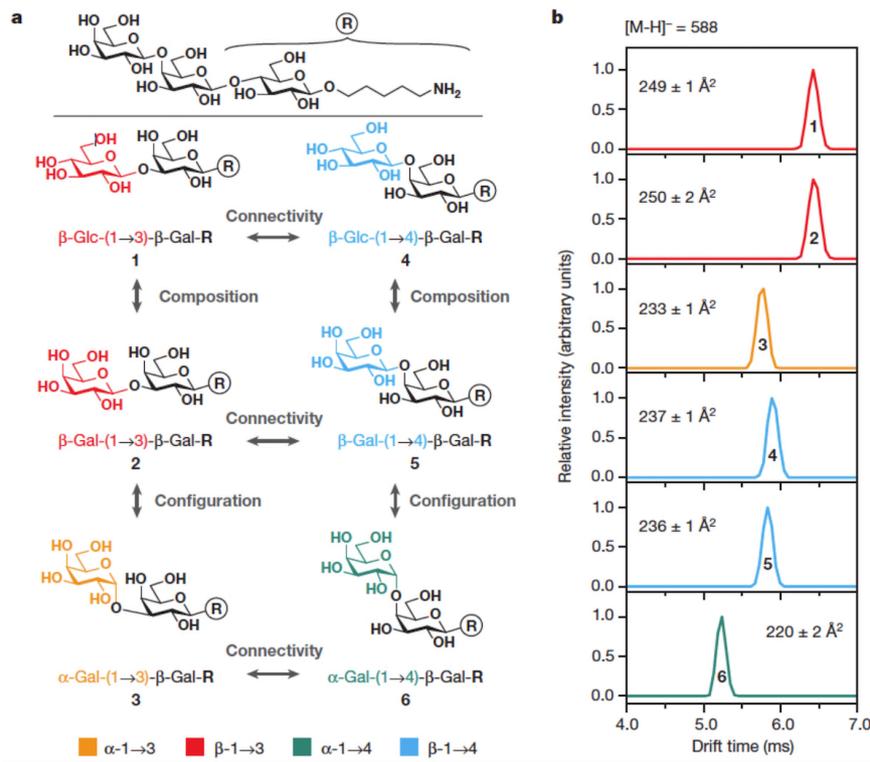
Carbohydrates form one of the major classes of biological macromolecules in living organisms, but structural analysis and the quality control of carbohydrate structures represent a major challenge due to the frequent occurrence of isomers that are difficult to distinguish using established techniques.

Changes in protein glycosylation are frequently identified in the context of diseases. For example, alterations in N-glycan profiles from blood plasma have been found to correlate with pathological states, such as diabetes type II, inflammation, and several types of cancer. However, in most clinical settings the glycosylation status of proteins is not determined due to the lack of tools that allow obtaining this information in sufficient specificity and sensitivity within the standard capacities of a haematology or clinical laboratory.

The availability of reliable, robust, rapid and sensitive workflows and technologies for sample preparation, data acquisition and automated analysis that can be handled on a routine basis would be key for the analysis of complex carbohydrate structures in the context of quality control or diagnostic tools.

#### Technology

Scientists of the Max Planck Society and of the Freie Universität Berlin developed a novel, highly sensitive and fast method for unambiguous determination of the composition, connectivity and configuration of glycans by ion mobility-mass spectrometry (IM-MS) in negative ionization mode.

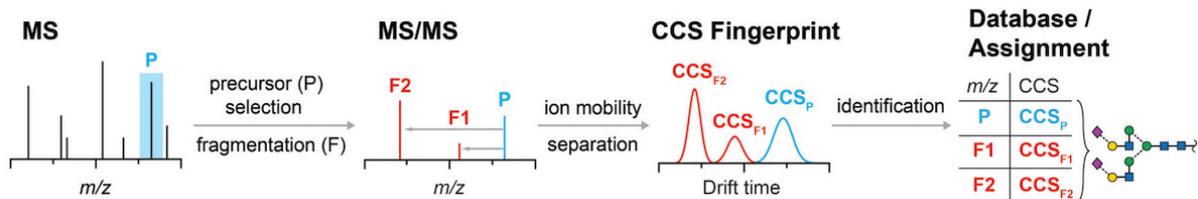


**Figure 1:** Structure and IM-MS data of trisaccharides 1-6.

a) The synthetic trisaccharides share the same disaccharide core, and differ merely in the composition, connectivity, or configuration of the last monosaccharide building block.

b) IM-MS drift-time distributions for trisaccharides 1-6 as  $[M-H]^-$  ions. The values in Å<sup>2</sup> correspond to the estimated CCSs in the drift gas nitrogen and represent averages of three independent measurements. Although compositional isomers cannot be distinguished, connectivity and configurational isomers are clearly identified on basis of their CCSs.

By combining the rotationally averaged collision cross-section (CCS) information of an ion in a specific drift gas, a molecular property that under controlled conditions is independent of instrument parameters and that is correlated to the shape of an ion with  $m/z$  data, the structural identification of glycans and glycoconjugates can be achieved.



**Figure 2:** Workflow of a tandem MS experiment followed by ion-mobility separation. The drift times of certain fragments (F) can be more characteristic than the intact precursor ions (P) and allow database supported structural identification.

Sample and time requirements of IM-MS are similar to those of conventional mass spectrometry, so the additional information is obtained at no extra cost. Additionally, with this novel method samples can be analysed with concentrations as low as 0.1 % of the target carbohydrate, making it a highly sensitive approach that requires very low sample quantities.



Combined with a CCS-database this new IM–MS-based method is a powerful tool that drastically improves the accessibility to structural information of complex carbohydrates. Connectivity and configurational isomers can be separated efficiently with baseline resolution, and the relative content of isomeric impurities can be determined quickly and easily, which paves the way for routine applications like quality control or diagnostic glycan biomarkers.

## Literature

K. Pagel, P.H. Seeberger, J. Hofmann, H.S. Hahm: "Identification of carbohydrate anomers using ion mobility–mass spectrometry"; *Nature*, Vol 526, pages 241+ , 8 October 2015

K. Pagel, J. Hofmann: "Glycan Analysis by Ion Mobility–Mass Spectrometry"; *Angew. Chem. Int. Ed.* 2017, 56, 8342 – 8349

## Patent Information

PCT priority application filed: WO2017036545 A1, national in US and CA.

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