SHEDDING LIGHT ON *O*-GLYCANS: DIFFERENTIATING GLYCAN ISOMERS BY THEIR GAS-PHASE STRUCTURE

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O-glycosylation is a common post-translational modification that is essential for the defensive properties of mucus barriers. Incomplete and altered *O*-glycosylation is often linked to severe diseases, such as cancer, cystic fibrosis, and chronic obstructive pulmonary disease. However, *O*-glycans are often present as complex mixtures containing multiple isomers that can be difficult to distinguish. Chromatographic separation of isomers is time-consuming and assignment by tandem-mass spectrometry remains challenging.
Here, we develop a glycomics workflow for separating and identifying mucin-type *O*-glycans based on trapped ion mobility mass spectrometry. Compared to LC-MS, the acquisition time is reduced from an hour to two minutes. To test the validity, the workflow was applied on sputum samples from cystic fibrosis patients to map *O*-glycosylation features associated with disease. However, separation because more challenging with increasing glycan complexity. To address this problem, we investigate the use of cryogenic infrared spectroscopy and provide the first data on *O*-glycans. Here, we uncover highly diagnostic features of negative ion mode spectra of glycans that help elucidate the structural motifs. A future perspective for the integration of cryogenic infrared spectroscopy in *O*-glycomics is provided.

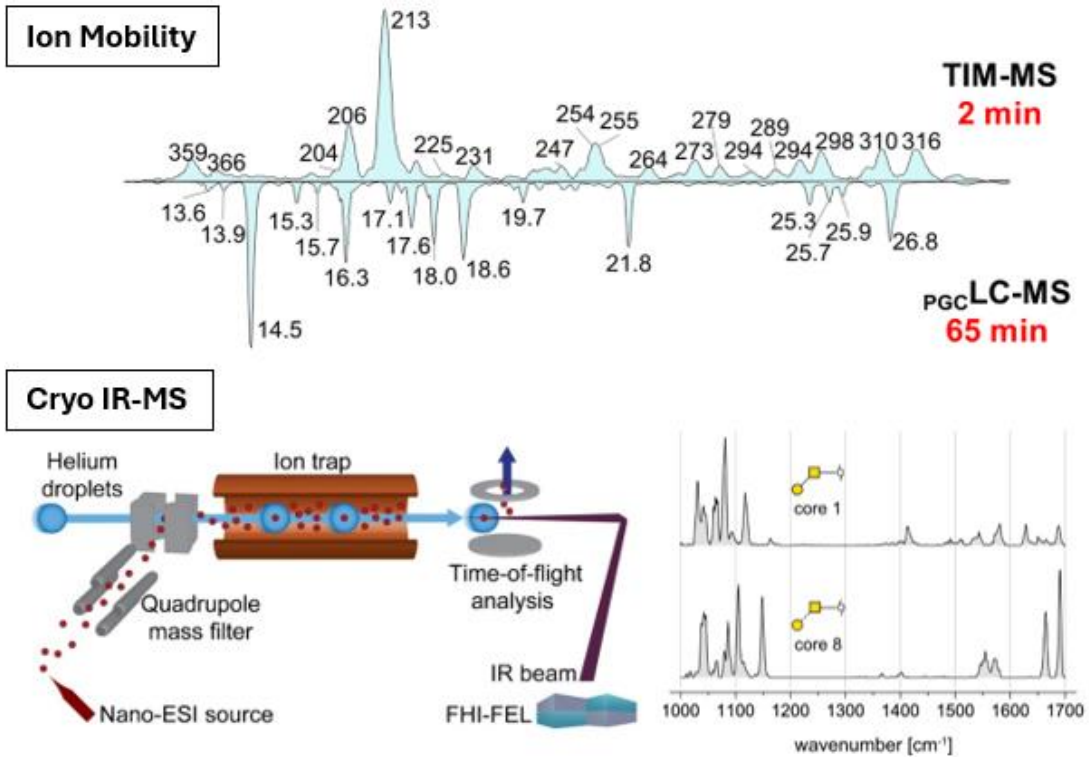

Figure 1. Top) Spectra of Trapped Ion Mobility Spectroscopy compared with traditional PGCLC. Bottom) Set-up for Cryogenic Infrared Spectroscopy and spectra for O-glycan core structures.