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Protein glycosylation probed by native MS

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High-resolution Fourier transform mass spectrometry (FTMS) combined with native electrospray ionization provides direct access to the proteoform and glycoform heterogeneity of intact glycoproteins. As a defined model system, the therapeutic antibodies adalimumab and trastuzumab were analyzed to test the ability of native MS to resolve Fc glycosylation variants with high mass accuracy. In parallel, human serum transferrin was investigated as a representative plasma glycoprotein with multiple N-glycosylation sites. The native mass spectra reveal a broad distribution of glycoforms and allow relative quantification of the dominant species, complementing NMR and UHPLC-based glycan profiling. These results highlight the utility of native FTMS for assessing microheterogeneity in glycoproteins, both in purified therapeutic antibodies and in proteins directly isolated from human serum.

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