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Comprehensive N-Glycan Profiling in Cancer Research: Past, Present and Future

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Summary

The intimate knowledge of aberrant glycosylation associated with human cancers was sparse until the first years of this century, when new analytical methodologies based on capillary LC, CE and the electrospray and MALDI mass spectrometry started to contribute to glycomic and glycoproteomic capabilities. The N-glycans immediately became the preferred target of glycomic studies because they were methodologically easier, but most importantly, their structural diversity and some known biosynthetic pathways have made N-glycans the perceived "zip codes" of the respective glycoproteins and their cellular environments. The first glycomic studies reported in the literature by different groups were often mutually inconsistent for either methodological reasons or differences in sample source and treatment. The methodologies matured within the next decade and more meaningful sets of clinical samples became available. Microderivatization and sample preconcentration techniques have been emphasized by our research group as the adjuncts to mass spectrometry and CE-LIF detection as demonstrated in examples of the studies pertaining to prostate cancer, pancreatic cancer, different types of breast cancer, and the profiles obtained from sera and tissues of ovarian cancer patients. As the result of gradual methodological improvements, some 60-90 N-glycans can be routinely monitored in different sample types and then statistically correlated with cancer conditions. However, with the more comprehensive sample isolation and simple group separation approaches, over 220 N-glycans can be identified, including the structural details associated with the isomerism of fucosyl and sialyl residues.

Some seemingly important glycans have been structurally elucidated within these profiles: paucimannosidic glycans; hyperfucosylated structures; multiply-branded glycans with three different sialyl linkages; and glycans with sulfation. The importance of the sample repositories, clinical information and medical collaborations cannot be overstated. To advance further the potential of glycomics for the sake of early diagnosis and prognostic evaluations will necessitate simplified measurements and enhanced sample throughput.