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Editorial

# The promise of glycomics for discovery of new biomarkers

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*Biomarkers: "Cellular, biochemical, molecular (genetic and epigenetic) alterations by which a normal, abnormal, or simply biologic process can be recognized, or monitored" and is "measurable in biological media, such as in tissues, cells, or fluids" – National Cancer Institute.*

Glycosylation, the attachment of carbohydrates to a protein or lipid, is the most abundant and structurally complex post-translational modification taking place in cells. Approximately two percent of the human genome codes for proteins involved in the glycosylation pathways that modify proteins and lipids. Carbohydrates themselves can be modified in multiple ways, undergoing for example acetylation, sulfation, methylation, phosphorylation, or sialylation. This results in a cellular glycan repertoire composed of vastly diverse and information-rich molecules. Glycans are central to numerous intra-cellular and inter-cellular processes including cell growth, differentiation, adhesion, and cell-cell recognition. To date ninety nine distinct human glycosylation disorders, many affecting multiple organ systems, have been identified. The extent of cellular glycosylation is dynamic, changing in response to the phenotype, metabolic state, and developmental stage of the cell. Changes in the expression of one's cellular glycan profile and the synthetic enzymes involved in their synthesis, as well as the repertoire of one's serum anti-glycan antibodies, are observed during cellular transformation and metastasis. For example, changes in N-glycan branching, the extent of sialylation or the rate of glycosylation of mucins, the over expression of sialylated gangliosides, and loss of expression of glycosylphosphatidylinositol (GPI), have all been correlated with malignant disease and its progression. This makes glycans promising molecules for the discovery of biomarkers to detect and monitor disease. However, until recently the study of carbohydrates as potential biomarkers has suffered from a lack of tools and technologies capable of carrying out rapid, robust analysis of structural and functional changes in cellular glycans, anti-glycan antibodies, and serum glycoproteins and glycolipids. The development of glycan array technology for determining the binding specificity of glycan binding proteins and serum anti-glycan antibodies, and advances in high-throughput analytical technologies capable of defining glycan structure, are now opening up new avenues for the discovery of glycan biomarkers with specific prognostic and diagnostic value. This special issue of *Cancer Biomarkers* will review the clinical findings and genetic and glycobiologic basis of glycosylation disorders, and the need for better serum based diagnostic biomarkers, beyond the presently used blood test for N-linked glycan disorders. New glyco-analytical tools for study of glycosylation changes in serum glycoproteins and how such data can improve our understanding of disease pathways and lead to discovery of pre-clinical and clinical glycan based disease biomarkers will be discussed. Likewise, the use of glycan array technology to identify new disease biomarkers, and the power of these arrays to determine carbohydrate binding specificity for use as a diagnostic tool, using flu as a model system will be presented. Finally, we will look at the presence of glycosylphosphatidylinositol anchored proteins in serum and how they may serve as biomarkers for detection of cancer, and how truncation of O-glycans (expression of the tumor-associated carbohydrate antigen Tn and/or Sialyl Tn antigen) through genetic and epigenetic pathways, or metabolic regulation results in malignant disease.

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