Rise of Systems Glycobiology and Personalized Glycomedicine: Why and How to Integrate Glycomics with Multiomics Science?

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Abstract

Glycomics is a rapidly emerging subspecialty of system sciences that evaluates the structures and functions of glycans in biological systems. Moreover, glycomics informs allied scholarships such as systems glycobiology and personalized glycomedicine that collectively aim to explain the role of glycans in person-to-person and between-population variations in disease susceptibility and response to health interventions such as drugs, nutrition, and vaccines. For glycomics to make greater, systems-scale, contributions to biology and medical research, it is facing a new developmental challenge: transition from single omics to multiomics integrative technology platforms. A comprehensive map of all possible connections between glycomics and other omics types has not yet been developed. Glycomics aims to discover a complex interplay of molecular interactions; however, little is known about the regulatory networks controlling these complex processes. In addition, the glycomics knowledgebase is presently scattered across various publications and databases, and therefore does not enable a holistic or systems view of this study field. Therefore, researchers are not always aware, for example, that a given analyzed genetic locus is linked with glycans, and that there are also glycomics determinants of complex phenotypes in health and biology. This review presents several published examples of glycomics science in association with other omics levels, such as genomics, transcriptomics, proteomics, metabolomics, epigenomics, ncRNomics, lipidomics, and interactomics. I also highlight the salient knowledge gaps and suggest future research directions. Understanding the interconnections of glycomics with other omics technologies will facilitate multiomics science and knowledge integration, enhance development of systems glycobiology and personalized glycomedicine.

Keywords: systems glycobiology, glycome, glycomics, multiomics, personalized medicine, personalized glycomedicine

Introduction

GLYCOMICS IS ONE OF THE LATEST omics system science fields that evaluates the structures and function of glycans in biological systems (Adua et al., 2017). While there have been early hints that integration of multiple omics fields with glycomics might offer new system-scale insights in integrative biology (Ly et al., 2010), a current discussion is warranted on the ways in which the emerging glycomics technologies can usefully be combined with other omics knowledge and technologies such as genomics, proteomics, metabolomics, and others yet to emerge in the near future (Fig. 1). Moreover, glycomics informs other crucial schol-

arships such as systems glycobiology and personalized glycomedicine that collectively aim to explain the role of glycans in person-to-person and between-population variations in disease susceptibility and response to health interventions such as drugs, nutrition, and vaccines.

Glycan is a compound consisting of a large number of monosaccharides linked glycosidically (oligosaccharides or polysaccharide) or a carbohydrate portion of glycoconjugates, such as glycoprotein, glycolipid, or a proteoglycan. Glycome is the entire complement of glycans or glycoconjugates in a cell, tissue, or organism. Glycoside is a molecule in which a sugar is bound to another functional group (to another glycan or an aglycone) through a glycosidic

FIG. 1. Glycomics technologies could be combined with other omics knowledge and technologies such as genomics, proteomics, metabolomics, and other emerging omics types, therefore enabling a shift from single omics to multiomics approach.

bond. A glycosidic bond is a type of covalent bond that joins a carbohydrate (sugar) molecule to another group, which may or may not be another carbohydrate. Various glycosidic bonds are known: S-, N-, C-, and O-glycosidic bonds (Bennun et al., 2016; Reily et al., 2019).

Glycosylation is a form of cotranslational and post-translational modification, and it is the enzyme-catalyzed covalent attachment of a carbohydrate to a polypeptide, lipid, polynucleotide, carbohydrate, or other organic compound, generally catalyzed by glycosyltransferases, utilizing specific sugar nucleotide donor substrates. Glycosyl transfer can also occur to protein residues, usually to tyrosine, serine, or threonine to give O-linked glycoproteins, or asparagine to give N-linked glycoproteins. Glycoside hydrolases or glycosidases are enzymes that break glycosidic bonds (Reily et al., 2019).

Glycogenes (also termed glycan genes) are genes, involved in glycan biosynthetic pathways. For example, *MGAT3* is a glycogene encoding for a glycosyltransferase mannosyl (beta-1,4-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase. According to the latest release of the HGNC (HUGO gene nomenclature committee) database, there are 210 genes annotated within the gene group glycosyltransferases. They are classified into 26 subgroups and include genes such as *OGT*, *MGAT5*, and *ST3GAL1* (<https://www.genenames.org/data/genegroup/#!/group/424>) (Yates et al., 2017). For example, *OGT* (O-linked N-acetylglucosamine (GlcNAc) transferase) is the enzyme driving O-GlcNAcylation.

Assembly of glycome structures requires a coordinated activity of various proteins, such as glycosyltransferases and glycosidases (Agarwal et al., 2015). Glycocode also termed a sugar code is a coding system on the basis of carbohydrates (Gabijs et al., 2011). It has a large coding capacity since the theoretical number of oligomers formed by monosaccharides is much higher than that formed by using nucleotides or amino acids (Gabijs and Kayser, 2014). Contrary to proteins, glycan biosynthesis does not require a template, and its structure is catalyzed by various enzymes that attach or detach monosaccharides in the glycosylation processes, therefore making glycomics research more challenging than

proteomics or genomics (Adua et al., 2017). The variety and dynamic in glycome composition enables a quick response to environmental stimuli (Lauc et al., 2016).

Systems glycobiology is a subfield of systems biology, and is a holistic approach to reveal complex glycosylation process and relations among its components. It aims to provide a more complete glycome overview based on glycan annotation and also on other aspects, such as enzymatic levels, glycans abundances, biosynthetic pathways, and associated omics data sets. Systems glycobiology approach is based on combining multiple glycomics data sets with other omics data using glycoinformatics to elucidate insights on glycosylation process from multiple data sets (Bennun et al., 2016).

Glycosylation is involved in both normal physiology and disease development (Varki, 2017). Aberrant glycosylation is a feature of several diseases. Differential glycosylation patterns could distinguish between disease and health state, and serve as stratification biomarkers (glycobiomarkers) in personalized medicine (Reily et al., 2019). Glycobiology and glycopathology will therefore enable several new medical implications (Gabijs and Kayser, 2014). Holistic insights into the structure and function of the glycome can be applied to therapy development, fine-tuning immunological responses and the performance of therapeutic antibodies and boosting immune responses, therefore greatly contributing to the development of the emerging field of glycomedicine (Reily et al., 2019).

Glycan arrays offer many applications in basic biochemical research to biomedical applications (Geissner and Seiberger, 2016). Shotgun glycan microarrays extended the defined glycan microarrays to a platform that supports functional glycomics analyses glycome (Smith et al., 2019). In addition, cell-based array resource has been developed, which displays the human glycome in a natural glycoconjugate and cell-surface context and will enable deeper understanding of the many biological roles of the glycome (Narimatsu et al., 2019). However, multiplatform and multiomics technologies are expected to further deepen our understanding of molecular mechanisms.

Integrating Glycomics with Other Omics Technologies and Knowledge

Systems glycobiology is a study field that aims to characterize cellular glycosylation processes based on integrating various omics data (Bennun et al., 2016). Integrating biomarkers across omics platforms has been shown to improve prediction accuracy. The integration of glycomics with other types of biomarkers offers further possibilities for innovation in diagnosis and treatment of diseases. For example, multivariate models consisting of different omics data (DNA methylation, transcriptomic, proteomic, and glycomics) obtained from analyses on different biomaterials have been shown to improve accuracy for prostate cancer risk stratification (Hart and Copeland, 2010; Murphy et al., 2018).

The first step toward classification of these complex genomics information according to omics levels was enabled by proposed taxonomy of multiomics science (Pirih and Kunej, 2017) and extended in previous studies (Pirih and Kunej, 2018; Redenšek et al., 2018) (Fig. 2). As other omics types, glycomics could be studied at a single locus or pathway, or at the whole genome level (Pirih and Kunej, 2018). Before multiomics data integration, data should first be sorted

FIG. 2. Glycomics in the context of multiomics taxonomy.

according to the separate omics levels. The following chapter presents selected examples of glycomics and its interaction with other omics levels in association with various molecular mechanisms and phenotypes.

Genomics—DNA Level

Sequence variants could be associated with glycomics at several ways. For example, they could cause gain or loss of a glycosylation site. Prostate cancer risk-associated single-nucleotide polymorphism has been shown to affect prostate-specific antigen (PSA) glycosylation and its function. Functional analysis showed that the missense variant rs61752561 affects PSA stability and structural conformation, and creates an extra glycosylation site (Srinivasan et al., 2019). Moreover, Fan et al. (2018) computationally identified cancer somatic variants causing potential gain or loss of glycosylation.

Beside short variants, structural variants and cytogenetics abnormalities could be associated with glycomics. Glycome expression has been shown to be associated with chromosomal aberrations. Cytogenetic aberrations t(11;14), t(4;14), hyperdiploidy, 1q21 gain, and 13q14 deletion have been associated with glycogene expression patterns in multiple myeloma (Moehler et al., 2013). Analysis of genetic variants associated with glycosyltransferases is of special importance since a single glycosyltransferase can glycosylate several proteins. Therefore, a single change in enzyme activity can affect the function of many glycoproteins. Thus, a genetic or epigenetic variant may have a pleiotropic effect on glycosylation, and can affect several downstream pathways and influence the cell metabolism on multiple levels (Vojta et al., 2016).

Transcriptomics—RNA Level

Several glycomics studies have been performed at the transcriptome level either at a single locus or using a microarray technology in human and animal models in associ-

ation with different phenotypes. Mining The Cancer Genome Atlas (TCGA) altered expression of a cancer-associated glycosyltransferase ST6GAL1 was identified in colorectal cancer (CRC) (Venturi et al., 2019). GLYCOv2 glycogene microarray technology was used to identify the differentially expressed glycosylation-related genes in healing mouse corneas (Saravanan et al., 2010).

Of 243 glycan-biosynthesis pathway genes, 60 showed a significantly higher, 20 a lower expression in myeloma compared with normal plasma cell samples (Moehler et al., 2013). Meta-analysis of prostate cancer gene expression data revealed a novel molecular signature, enriched for glycosylation enzymes (Barfeld et al., 2014). Expression of genes that control core fucosylation in hepatocellular carcinoma has been systematically reviewed (Norton and Mehta, 2019). Further systematic reviews and meta-analyses are needed to integrate published data to identify robust expression signatures for development of reliable biomarkers.

Glycoproteomics

Glycoproteomics is a study of glycoproteins, including their protein identities, sites of glycosylation, and glycan structures. Glycans contribute to protein function by modulating its function through alternative glycosylation; addition of different glycans to the same attachment site on the polypeptide chain (Lauc et al., 2016).

A large number of studies using different methodologies have been published in association with different phenotypes, such as breast, colon, liver, skin, ovary, bladder cancer, and neurological disorders and various structural alterations such as sialylation, fucosylation, degree of branching, and the expression of specific glycosyltransferases (Azevedo et al., 2017; Christiansen et al., 2014; Palmigiano et al., 2016). For example, cerebrospinal fluid N-glycoproteomics was used for early diagnosis in Alzheimer's disease. The study enabled one

to assess specific glycosylation patterns in patients and also suggested therapeutics targets, such as glycoenzymes (Palmigiano et al., 2016).

Simultaneous measurement of specific glycoforms combined with protein levels has been suggested to increase the diagnostic potential in pancreatic cancer (Llop et al., 2018). The majority of FDA-approved protein tumor markers currently used in clinical practice are glycoproteins, many of them showing glycosylation alterations in cancer (Lauc et al., 2016). Due to a large number of heterogeneous published results, systematic integrative reviews of the literature are needed to monitor and guide the development of the study field.

Metabolomics

Metabolomics is a study field that evaluates changes in the metabolome of an organism by exploring the set of small molecules; metabolites. Konjevod et al. (2019) reviewed metabolomic and glycomic findings in post-traumatic stress disorder. The authors suggested integration of these biomarkers with additional omics markers to increase understanding of the biological alterations of this condition.

Wang et al. (2016) performed integrative analysis of proteomic, glycomic, and metabolomic data for liver cancer biomarker discovery. An improved performance was observed by integrative analysis in comparison with separate omics data (Wang et al., 2016). Metabolome and glycome reflect the physiological and pathological conditions in individuals. Some glycans are small molecules, which enables their easy quantification like metabolites (An et al., 2009). A valuable resource for biomarker innovation is the Human Metabolome Database (HMDB), which is the most comprehensive repository of metabolites and could therefore greatly enhance novel biomarker discovery in glycomics (Wishart et al., 2007).

Epigenomics

DNA methylation, histone tail modifications, and RNA-mediated regulation of gene expression are well-known epigenetic mechanisms. Epigenetic modification of genes involved in protein glycosylation has been reported in several studies. However, complex interactions link glycomics and epigenomics. Namely, in contrast with the epigenetic regulation of glycogenes, glycosylation itself epigenetically regulates transcription of other genes. The only form of glycosylation found in the mammalian nucleus, O-GlcNAc, was identified as an epigenetic, histone mark, indicating that glycosylation itself epigenetically regulates gene transcription (Kizuka, 2015).

DNA Methylation

It has been shown that glycogenes change expression in cancer through aberrant methylation (Vojta et al., 2016). In addition, promoter methylation of the *MGAT3* and *BACH2* genes correlates with the composition of the immunoglobulin G glycome in inflammatory bowel disease (Klasić et al., 2018). A complete set of glycogenes could now be screened for their potential regulation by DNA methylation and then if this epigenetic change could be affected with sequence variants.

Histone Modifications

O-GlcNAc glycosylation (O-GlcNAcylation) is an epigenetic mark, and it was suggested to be pivotal in the modu-

lation of chromatin remodeling and in the regulation of gene expression by being part of the histone code (Dehennaut et al., 2014). Covalent post-translational modifications of histones (methylation, acetylation, ubiquitylation, and O-GlcNAcylation) are dynamically regulated by the interplay of enzyme pairs that add and remove these modifications (Kizuka, 2015).

NcRNomics

Noncoding RNAs are divided into short (<200 bp) and long noncoding RNAs (lncRNAs) (>200 bp) according to their length. RNA-mediated regulation of gene expression is one of the epigenetics mechanisms, but due to its extent and heterogeneity it is frequently studied as a separate omics type.

MiRNomics

MicroRNAs (miRNAs) belong to a group of short ncRNAs. Classification of miRNA-related genetic variations is challenging because miRNAs interact with different genomic elements and are studied at different omics levels, including glycomics. MiRNA-associated genetic variability could be studied at miRNA genes and their upstream regulatory elements, genes encoding miRNA silencing machinery (Dicer, Drosha), and miRNA targets (Hrovatin and Kunej, 2018). These categories may also present crossroads for interconnections with glycomics. Mapping post-transcriptional regulation of the human glycome revealed that a subset of miRNAs are involved in regulation of the glycode (Agrawal et al., 2014) and could therefore be termed glyco-miRNAs.

Glycomic analysis platform, lectin microarray, was used to identify glycosylation signatures in the NCI-60 cell panel. miRNA regulators were then mapped onto genes in glycan biosynthetic pathways that generate the observed glycan structures. Global glycosylation network regulated by miRNAs provides a link between miRNA-mediated control of cell phenotype and the glycome (Agrawal et al., 2014). Beside miRNAs, several other types of short ncRNAs are known, such as siRNAs, snoRNAs, and piRNAs, and should be systematically studied in association with glycomics.

LncRNomics

lncRNAs have been implicated in a range of developmental processes and diseases; however, they have not yet been systematically studied in association with glycogenes. Most studies focused on selected lncRNAs, such as long intervening/intergenic noncoding RNAs (lincRNAs) and ultraconserved regions (UCRs). For example, lincRNA has been linked with O-glycosylation involved in CRC progression. LINC01296/miR-26a/GALNT3 axis contributes to CRC progression by regulating O-glycosylated MUC1 through PI3K/AKT pathway (Liu et al., 2018). In addition, long noncoding transcript from UCRs, termed transcribed-UCRs (T-UCRs), has been shown to reside within *OGT* gene (Ferdin et al., 2013).

Hypoxia-upregulated T-UCR named HINCUT (hypoxia-induced noncoding ultraconserved transcript) was proposed to be critical for optimal O-GlcNAcylation of proteins in oxygen deprivation in cancer. The current version of the HGNC database includes 438 lncRNAs (<https://www.genenames.org/data/genegroup/#!/group/788>) and could be systematically analyzed for their potential involvement in regulation of glycome.

Glycolipidomics

Glycolipidomics is a study field focused on identification and quantification of glycolipids. Glycolipids have potential as specific biomarkers for various physiological and pathological processes. They have been shown to be involved in development of neurological and neurodegenerative diseases, such as Parkinson's disease, Alzheimer's disease, Lewy body dementia, and frontotemporal dementia. In addition, cancer-associated glycosphingolipids have been used as markers for diagnosis and targets for immunotherapy of malignant tumors (Furukawa et al., 2019). In addition, cancer-associated glycosphingolipids have been used as markers for diagnosis and targets for immunotherapy of malignant tumors (Furukawa et al., 2019). Recent advancements in glycolipid biomarker discovery by mass spectrometry are reviewed in Dehelean et al. (2019).

Interactomics

Interactome is a whole set of molecular interactions in cell including glycan interactions. Binding between glycans and glycan-binding proteins (GBPs) was shown to be involved in almost all physiological and pathophysiological processes, including cell recognition and signaling, immune response, infections, cancer, and neurodegenerative disorders. These interactions could now be studied using high-throughput techniques (Kitov et al., 2019). Lectins are GBPs and are cataloged in the UniLectin3D a database with curated information on 3D structures and interacting ligands (Bonnardel et al., 2019). The interactions between lectins and glycans on plasma membranes have emerged as important regulatory factors in corneal biology and pathophysiology, including corneal infection and inflammation (AbuSamra and Argüeso, 2018).

The complete protein–glycan interactions (protein–glycan interactome) have not yet been determined or estimated (Cummings and Pierce, 2014). An estimation of the number of these interactions is an important study question for future studies. Bioinformatics tool GenProBiS (Konc et al., 2017), for example, enables protein–protein, protein–nucleic acid, and protein–compound binding site analysis, including glycosylation and other post-translational modification sites. Moreover, it maps sequence variants to protein structures. Further development of advanced bioinformatics tools enabling big data analyses will enable prioritization of the targets for experimental validation and substantially contribute to the development of the interactomics field.

Other Omics Types

Several other omics types need to be systematically reviewed in association with glycomics in future studies, for example, regulomics and comparative genomics. Glycomics is involved in a complex interplay of molecular interactions; however, little is known about the regulatory networks controlling these complex processes. Transfer of glycomics knowledge gained from animal models (comparative glycomics) is also one of the research directions.

Beside basic (classic) omics types, omics applications need to be reviewed, such as pharmacogenomics, environmental omics, nutrigenomics, and iatronics. Glycans have a large potential for therapeutics as many recombinant pharmaceuticals, like thera-

peutic monoclonal antibodies, are glycoproteins (Lauc et al., 2016). In addition, *O*-GlcNAcylation is a post-translational modification that links nutrition to epigenetics. Uridine diphosphate-GlcNAc (UDP-GlcNAc) and *O*-GlcNAcylation are therefore considered as sensors of the nutritional state of the organism (Dehennaut et al., 2014).

Multiomics

The glycomics study field has shifted from single locus to whole genome-level study approaches. Moreover, it has shifted from single omics to integrated omics understanding of disease mechanisms. Integration of the transcriptome and glycome was performed for identification of glycan cell signatures (Bennun et al., 2013). A number of studies with integration of multiple platforms are expected in the near future as they are increasingly produced. The number of included omics levels into integrative analyses is expected to increase as well. Data from 13 omics layers including glycomics were synthesized with the aim to enable a step toward a systems view on pathological mechanisms and for prioritization of novel potential biomarkers in Parkinson's disease and asthma (Pecak et al., 2018; Redenšek et al., 2018).

Mass spectrometry imaging has emerged as a powerful tool for the detection of various molecules, including proteins, peptides, glycans, metabolites, phospholipids, and glycolipids, in tissue samples, and therefore presents an important tool for multiomics studies (Xu and Li, 2019). The integration of multiple data sets from different omics levels represents an important application of systems biology for understanding complex cellular processes involved in glycobiochemistry.

Bioinformatics Tools and Databases

Glycoinformatics is a field of informatics that studies glycome. Bioinformatics tools are now needed to collect glycomics data and enable the user to search, display, and connect with other sources of related proteomics, genomics, and interactomics information. GlyConnect (<https://glyconnect.expasy.org/>) is the central platform for glycoinformatics. It has been developed to gather, monitor, integrate, and visualize glycomics data and to integrate multiple data types (Alocchi et al., 2019). Major web-based glycan resources are reviewed in Bennun et al. (2016) and include the following: GlycomeDB, GlycoSuiteDB, Japan Consortium for Glycobiochemistry and Glycotechnology Database (JCGGDB), and Complex Carbohydrate Structure Database (CCSD; CarbBank).

The current version of the Nucleic Acids Research (NAR) database lists 14 resources under the “Carbohydrates” subsection <https://www.oxfordjournals.org/nar/database/subcat/4/12> (Rigden and Fernández, 2019) and presents a starting point for glycomics research. To facilitate the data visualization and visual comparison of glycan array data, GLAD (GLYcan Array Dashboard) tool has been developed, which enables one to visualize and mine glycan array data (Mehta and Cummings, 2019).

International Collaborative Initiatives

International collaborative initiatives have already contributed to development of resources in technologies in glycomics such as Consortium for Functional Glycomics (CFG) and the National Center for Functional Glycomics

(NCFG). Data for >3900 experiments have been made public by the CFG (www.functionalglycomics.org/) (Mehta and Cummings, 2019). The Human Glycome Project (HGP) <https://human-glycome.org/> supports individual researchers by sharing resources and experiences, as well as coordinating research activities on a global level.

Challenges and Future Directions

Despite several recent advancements in the glycomics field, a systematic map of all possible connections between glycomics and other omics types has not yet been developed. Glycomics is involved in a complex interplay of molecular interactions; however, little is known about the regulatory networks controlling these processes. On the contrary, several physiological and pathological mechanisms are known, but the knowledge is scattered across various publications and databases, and therefore does not enable a holistic view of this study field. Therefore, researchers are not always aware that the analyzed genetic locus is linked with glycans and that a result of the study is interconnected with glycomics level. Integrating glycomics with other omics levels is a challenge at one locus, and even larger task at the genome-wide level.

Importantly, the present literature analysis also revealed several salient knowledge gaps and future directions in the glycomics field. I highlight them below for future consideration of scholars in the field of glycomics specifically, and omics system sciences broadly:

- (1) Development of a detailed map of all connections between glycomics and other omics types, such as epigenomics, miRNomics, proteomics, lipidomics, and interactomics
- (2) Systematic analysis and prioritization of all known sequence variants, associated with glycomics, for example, located within genes encoding for glycosyltransferases and glycosidases or located within glyco-miRNA target sites
- (3) Harnessing or finding novel utilities for heterogeneous published data and their integration with glycomics
- (4) Development of multiplatform approach including high-throughput *N*-glycan analysis techniques
- (5) Development of multiomics biomarker panels, including glycans
- (6) Further extending of systems biology with systems glycobiology and systems glycopathology
- (7) Integration of personalized glycomedicine into personalized medicine
- (8) Hands-on laboratory and bioinformatics training in the methods of glycomics
- (9) Development of an initiative for reporting standardization in glycomics
- (10) Performing systematic reviews and meta-analyses to integrate published data to identify potential new biomarkers, to identify knowledge gaps and guidelines for future studies.

Conclusions

Glycomics is a very broad study field and interacts with several omics types. However, it is only one of the omics

levels of a complex regulatory interplay, consisting of a large number of genomics elements. Further development of high-throughput analysis techniques and bioinformatics tools is expected in the future and will enable to integrate all available glycomics data into a single map, which will enable biomarker development and identification of potential new therapeutic targets.

The present review presents only selected examples how glycomics overlaps with other omics types and presents a framework for further systematic reviews. Integration of all published data related to glycomics is very extensive for one research group. Therefore, a consortium leading the community such as HGP is of importance to organize the development of the complete glycomics resource, and to coordinate planning of research of glycobiology and personalized glycomedicine. Research developments indicate that glycomics should be included in an integrative multiomics approach toward development of robust disease biomarkers enabling patient-tailored clinical decisions.

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Abbreviations Used

ARRS = Slovenian Research Agency
 CCSD = Complex Carbohydrate Structure Database (CarbBank)
 CFG = Consortium for Functional Glycomics
 CRC = colorectal cancer
 GBP = glycan-binding protein
 GLAD = GLycan Array Dashboard
 GlcNAc = N-acetylglucosamine
 HGNC = HUGO gene nomenclature committee
 HGP = The Human Genome Project
 HINCUT = hypoxia-induced noncoding ultraconserved transcript
 HMDB = Human Metabolome Database
 JCGGDB = Japan Consortium for Glycobiology and Glycotechnology Database
 lincRNA = long intervening/intergenic noncoding RNA
 lncRNA = long ncRNA
 miRNA = microRNA
 NAR database = Nucleic Acids Research database
 NCFG = National Center for Functional Glycomics
 ncRNA = noncoding RNA
 OGT = O-linked GlcNAc transferase
 PSA = prostate-specific antigen
 TCGA = The Cancer Genome Atlas
 T-UCR = transcribed-UCR
 UCR = ultraconserved region
 UDP-GlcNAc = uridine diphosphate-GlcNAc