

Technical Note

Updates to the Symbol Nomenclature for Glycans guidelines

Sriram Neelamegham^{1,2}, Kiyoko Aoki-Kinoshita³, Evan Bolton⁴,
Martin Frank⁵, Frederique Lisacek⁶, Thomas Lütteke⁷, Noel O’Boyle⁸,
Nicolle H Packer⁹, Pamela Stanley¹⁰, Philip Toukach¹¹, Ajit Varki¹²,
Robert J Woods¹³ and The SNFG Discussion Group¹⁴

²Department of Chemical & Biological Engineering and Medicine, State University of New York, 906 Furnas Hall, Buffalo, NY 14260, USA ³Glycan & Life System Integration Center (GaLSIC), Faculty of Science and Engineering, Soka University, 1-236 Tangi-machi, Hachioji, Tokyo 192-8577, Japan ⁴National Library of Medicine, 8600 Rockville Pike, Bldg. 38A, Room 8S810, Bethesda, MD 20896, USA ⁵Biognos AB, Generatorsgatan 1 / Box 8963, 402 74 Göteborg, Sweden ⁶Proteome Informatics Group, SIB Swiss Institute of Bioinformatics, Computer Science Department, University of Geneva, route de Drize 7, CH - 1227 Geneva Switzerland, and also Section of Biology, University of Geneva, Geneva, Switzerland ⁷GIP GmbH, Strahlenberger Str. 112, 63067 Offenbach, Germany ⁸NextMove Software, Innovation Centre, Cambridge Science Park, Milton Road, Cambridge, CB4 0EY, UK ⁹Department of Molecular Sciences, Faculty of Science & Engineering, Rm 307, Building E8C, Macquarie University, Sydney, NSW 2109, Australia ¹⁰Department of Cell Biology, Albert Einstein College of Medicine, 1300 Morris Park Ave, New York, NY, 10461, USA ¹¹Laboratory of Carbohydrate Chemistry, Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Leninsky prospect 47, Russia ¹²Glycobiology Research and Training Center, University of California, San Diego, La Jolla, CA 92093, USA, and ¹³Complex Carbohydrate Research Center, University of Georgia, 315 Riverbend Rd, Athens, GA, 30602, USA

¹To whom correspondence should be addressed: Tel: 716-645-1200; Fax: 716-645-3822; e-mail: neel@buffalo.edu

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Abstract

The Symbol Nomenclature for Glycans (SNFG) is a community-curated standard for the depiction of monosaccharides and complex glycans using various colored-coded, geometric shapes, along with defined text additions. It is hosted by the National Center for Biotechnology Information (NCBI) at the NCBI-Glycans Page (www.ncbi.nlm.nih.gov/glycans/snfg.html). Several changes have been made to the SNFG page in the past year to update the rules for depicting glycans using the SNFG, to include more examples of use, particularly for non-mammalian organisms, and to provide guidelines for the depiction of ambiguous glycan structures. This Glycoforum article summarizes these recent changes.

Key words: database, glycobiology, glycoscience, software, symbol nomenclature

SNFG

The Symbol Nomenclature for Glycans (SNFG) is a community-curated, broadly utilized standard for the depiction of glycans using various colored, geometric shapes (Varki et al. 2015). It has been

adopted by various publications including the journal *Glycobiology* (Haltiwanger 2016) and others listed at <https://www.ncbi.nlm.nih.gov/glycans/snfgorg.html>, and by major glycoscience databases (Table I). The historical background of the SNFG, which now spans

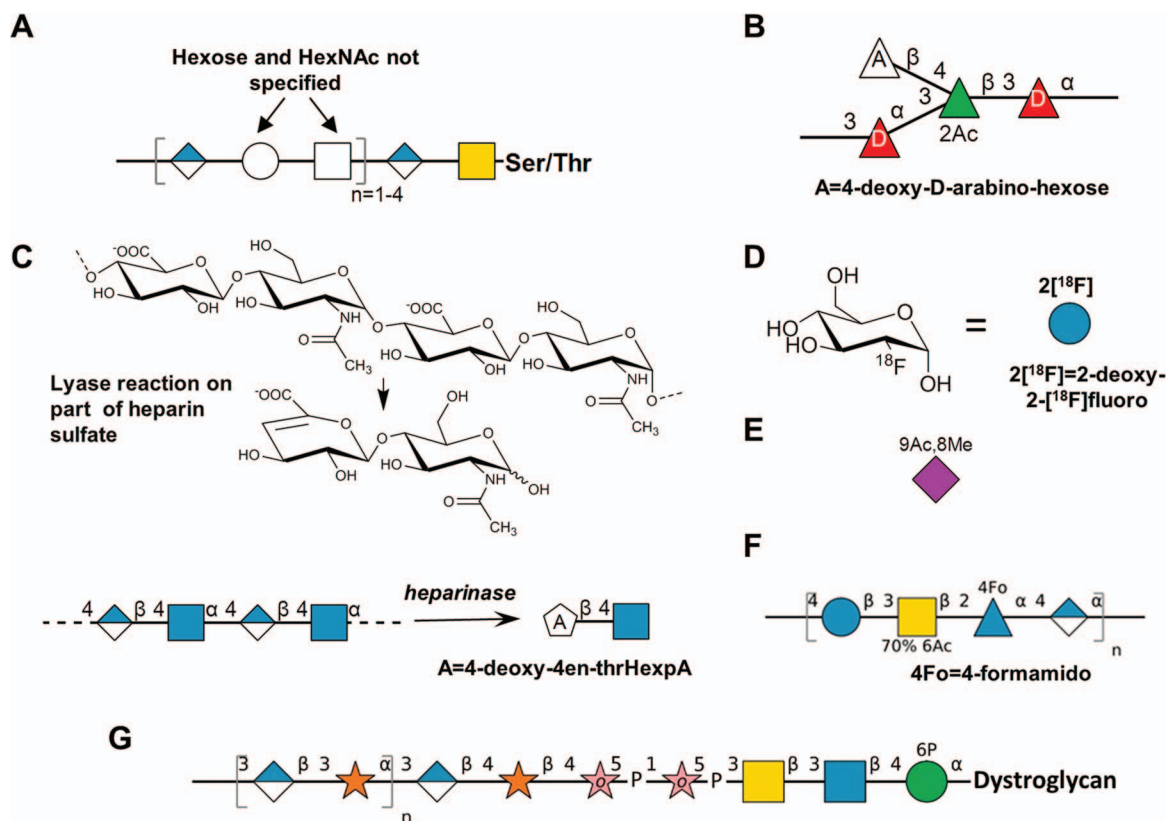


Fig. 1. Footnotes, white symbols and variable modifications in the SNFG. (A) *Drosophila* O-glycan with generic Hexose and HexNAc (Tiemeyer et al. 2015). (B) Bacterial glycan from *Citrobacter braakii* including D-Fucose, 2-O-acetylation and 4-deoxy-D-arabinohexose (a deoxyhexose variant; Katzenellenbogen et al. 2003). All rings are pyranose. (C) Use of pentagon with single non-italicized letter to depict product not defined by the SNFG (lyase reaction shown above sketch, adopted from Shaya et al. 2010). (D) Positron emission tomography tracer 2-deoxy-2-[^{18}F]fluoro- α -D-glucopyranose. (E) 9-O-acetyl-8-O-methyl-N-acetylneuraminic acid (Neu5,9Ac₂8Me). Purple diamond, Neu5Ac, already includes 5Ac modification. (F) O-polysaccharide from *Providencia alcalifaciens* with variable modification on GalNAc (Ovchinnikova et al. 2007). (G) Glycan chain of α -dystroglycan containing ribitol-5-phosphate and phosphate at 6-position of mannose (Kanagawa et al. 2016). The “o” in the pink star represents the alditol of the monosaccharide.

nearly 40 years, has been previously reviewed (Varki et al. 2015). Currently, the SNFG is hosted by the National Center for Biotechnology Information (NCBI) at the NCBI Glycans Page (www.ncbi.nlm.nih.gov/glycans/snfg.html), and it is curated by an international group of researchers in the field (see SNFG Discussion Group list). Additionally, various software programs for sketching glycans have been developed to support the implementation of this nomenclature (Table II).

The overall goal of the SNFG is (1) to facilitate communications and presentations of monosaccharides and glycans for researchers in the glycosciences and for scientists and students less familiar with the field; (2) to ensure uniform usage of the nomenclature in the literature, thus helping to ensure scientific accuracy in journal and online publications; and (3) to continue to develop the SNFG and its applications to aid wider use by the scientific community. With these goals in mind, updates have been made this year to the NCBI Glycans page that hosts the SNFG. Specifically, the footnotes to Table I at the SNFG page that include the rules for depicting glycans have been modified. No changes were made to the table. The footnotes are now organized into 10 themes in order to help streamline their use. These footnotes provide guidelines for (i) general usage of the SNFG, (ii) CMYK/RGB color codes, (iii) symbol colors and shapes, (iv) ring configurations, (v) bond linkage presentation, (vi) sialic acids, (vii) glycan modifications, (viii) amino substitutions, (ix) handling

ambiguous or partially defined glycans and (x) depicting non-glycan entities using SNFG renderings.

More examples have been included for non-mammalian species (Figure 1), with the realization that there is much greater diversity in monosaccharide composition and modifications in these organisms compared to vertebrates. This necessitates the need to engender greater flexibility with respect to SNFG use. To address this issue, several changes have been made.

First, white symbols of various shapes were previously used to define monosaccharides of unknown/undefined stereochemistry (white circle for hexose, type undefined, white diamond for deoxynonulosonic acids etc.). This usage of white symbols remains in the current revision. For example, Figure 1A depicts a *Drosophila* O-glycan that contains generic hexose and N-acetylhexosamine. However, while the white, flat hexagon was previously used to denote both heptoses and unknown monosaccharides, its usage is now restricted to depicting only unknown or partially defined monosaccharides.

Second, a single, non-italicized letter (A...Z) is now permitted inside white symbols to provide additional information about a monosaccharide that is not defined by a colored symbol. Footnotes/figure legends associated with these single letters convey structural details regarding this annotated symbol. When using the white symbol with a single letter, it is necessary to ensure that the chemical

Table I. SNFG compliant and actively maintained glycan databases^a

Name	Link	Contents	Reference
Asian Community of Glycoscience and Glycotechnology Consortium for Functional Glycomics Gateway	acgg.asia/db/	Includes glycan disease, glycogene, lectin frontier and curated protocols developed by the Japanese Consortium for Glycobiology and Glycotechnology and other collaborators	Maeda et al. (2015)
Carbohydrate Structure Database (CSDB)	www.functionalglycomics.org	Glycan array, Glycan mass spectrometry profiling, glycogene microarray and mouse phenotyping data repository	Raman et al. (2006)
CSDB_GT (CSDB Glycosyl-transferases)	csdb.glycoscience.ru/database	Manually curated bacterial, plant and fungal carbohydrate structure database	Toukach and Egorova (2016)
GLYCAM-Web	csdb.glycoscience.ru/gt.html	Manually curated database of glycosyltransferases with confirmed activity (in 2019, of <i>Escherichia coli</i> and <i>Arabidopsis thaliana</i>)	Egorova et al. (2019)
GLYCOSCIENCES.de	Glycam.org	Tools for predicting 3D structures of carbohydrates, glycoproteins and carbohydrate-protein structures	Kirschner et al. (2008)
Glycostore	glycosciences.de	Various tools and databases for glycobiology, with focus on 3D structures and references to related PDB entries	Bohm et al. (2019)
Glyco3D	glycostore.org	Glycan chromatographic retention properties	Zhao et al. (2018)
Glycomics@ExPASy	glyco3d.cermav.cnrs.fr/home.php	Family of databases covering the 3D features of mono-, poly- and oligo-saccharides, glycosyltransferases and lectins and glycosaminoglycan-binding proteins	Perez et al. (2015)
GlyCosmos	www.expasy.org/glycomics	Various glycomics tools developed at the Swiss Institute of Bioinformatics and links to other sites	Mariethoz et al. (2018)
GlyGen	glycosmos.org	Portal for glycoscience data resources and repositories	...
GlyYouCan	www.glygen.org	Computational and Informatics Resources for Glycoscience research	...
KEGG GLYCAN ^b	glytoucan.org	International glycan structure repository	Tiemeyer et al. (2017)
MatrixDB	www.genome.jp/kegg/glycan/	Glycan structures, relevant reactions and pathways	Kanehisa (2017)
MonosaccharideDB	matrixdb.univ-lyon1.fr/	Database of extracellular matrix protein, proteoglycan and polysaccharide interactions	Clerc et al. (2019)
SugarBindDB	monosaccharidedb.org	Monosaccharide database	Mariethoz et al. (2016)
UniCarb-DB	sugarbind.expasy.org	Pathogen Sugar-Binding Database	Mariethoz et al. (2016)
	unicarb-db.expasy.org	Glycomics mass spectrometry database	Campbell et al. (2014)

Note: ^aTable only lists databases that follow a majority of the SNFG nomenclature guidelines, not all glycoscience resources.

^bSNFG adoption in progress.

Table II. SNFG drawing software

Name	Purpose	Reference
3D-SNFG	3D adaptation of SNFG to visualize glycans in pdb structures (web based, implemented in VMD software)	Thieker et al. (2016)
3D-SNFG in LiteMol	Implementation of 3D-SNFG in LiteMol for 3D display of glycans	Sehna and Grant (2019)
DrawGlycan-SNFG	Converts IUPAC string to SNFG drawings (web based, stand-alone)	Cheng et al. (2017)
SugarSketcher	Drag and drop tool to sketch glycans (web based)	Alloci et al. (2018)
GlycanBuilder2	GlycanBuilder extended for rendering SNFG sketches (stand-alone)	Tsuchiya et al. (2017)

composition (and thus mass) of the entity corresponds to the composition of the selected white generic type. For example, the bacterial glycan in Figure 1B contains a deoxyhexose variant with known composition. A white triangle with letter “A” is used since this deoxyhexose is not defined by any colored SNFG symbol. A footnote is provided to explain the exact usage. In another case, if a monosaccharide has no equivalent representation in the SNFG table as in Figure 1C, a pentagon is used. In this case, heparinase action on a glycosaminoglycan results in a chemically defined product, but the generic type of the entity does not correspond to any of the standard white symbols in the SNFG table. Thus, a white pentagon is used with the letter “A” and an accompanying footnote.

Third, the rules for describing substituents have been reviewed and more examples are provided. For example, Figure 1D shows a commonly used fluoro-glucose analog, with a footnote providing a full explanation of the modification. Figure 1E illustrates a multiply-modified sialic acid, where the substituents are presented as a sequential/concatenated string. To the extent possible, abbreviations used to describe substituents should follow guidelines described in footnote 7 of the updated SNFG page. The presence of variable amounts of substituents may be indicated using the \pm symbol or by indicating % presence if known, e.g. “70% 6Ac” to indicate presence of 6Ac on 70% of a residue or repeating unit (Figure 1F). Less common substituents like “4Fo”, which are not among the standard monosaccharide modifications listed on the SNFG page, may also be indicated using footnote as illustrated. The final example illustrates the use of italicized “o” within a pink star to depict ribitol in an O-glycan that is found on mammalian dystroglycan (Figure 1G).

Please note that the meaning of single letter annotations in colored SNFG symbols is different from those in the white symbols. In the colored symbols, such annotations can only be used to denote either “D”/“L” configuration or ring closure information (“p”, “f” or “o” for pyranose, furanose and alditol, respectively). In white symbols, they are used to annotate details regarding generic monosaccharide types as discussed in the above examples. More exhaustive examples of SNFG usage can be found at the NCBI-SNFG page, Essentials of Glycobiology textbook (<https://www.ncbi.nlm.nih.gov/books/NBK310274/>) and the database resources listed in Table I.

Overall, the goal of the SNFG is to make the field of glycobiology more visual and readily accessible, especially for new users and the larger biomedical community. As we make progress in this endeavor, the group anticipates working with the Glycan Informatics Advisory Group (GlyAg, www.ncbi.nlm.nih.gov/glycans/glyag.html) to populate more glycan-related pages at the NCBI and to establish links between these pages and other database resources (Table I). Comments from the scientific community are welcome, including examples of SNFG implementation in databases and software resources.

Author contributions

¹⁴Other members of the SNFG Discussion group: Alan Darvill, University of Georgia, USA; Anne Dell, Imperial College London, UK; Bernard Henrissat, Centre National de la Recherche Scientifique (CNRS), France; Carolyn Bertozzi, Stanford University, USA; Gerald Hart, University of Georgia, USA; Hisashi Narimatsu, Research Center of Medical Glycoscience, Japan; Hudson Freeze, Sanford-Burnham-Prebys Research Institute, USA; Issaku Yamada, The Noguchi Institute, Japan; James Paulson, Scripps Research Institute, USA; James Prestegard, University of Georgia, USA; Jamey Marth,

University of California Santa Barbara, USA; JFG Vliegenthart, Bijvoet Center, Netherlands; Marilyn Etzler, UC Davis, USA; Markus Aebi, ETH Zürich, Switzerland; Minoru Kanehisa, Kyoto University, Japan; Naoyuki Taniguchi, Riken Global Research Cluster, Japan; Nathan Edwards, Georgetown University, USA; Pauline Rudd, National Institute for Bioprocessing Research & Training, UK; Peter Seeberger, Max-Planck-Institute of Colloids and Interfaces, Germany; Raja Mazumder, The George Washington University, USA; Rene Ranzinger, University of Georgia, USA; Richard Cummings, Harvard Medical School, USA; Ronald Schnaar, Johns Hopkins University School of Medicine, USA; Serge Perez, French National Centre for Scientific Research, France; Stuart Kornfeld, Washington University in St. Louis, USA; Taroh Kinoshita, Osaka University, Japan; William York, University of Georgia, USA; Yuriy Knirel, Russian Academy of Sciences, Russia

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Conflict of interest statement

None declared.

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