

The NIH Common Fund Glycoscience Program

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Douglas M. Sheeley, Sc.D.

January 25, 2024



National Institutes of Health

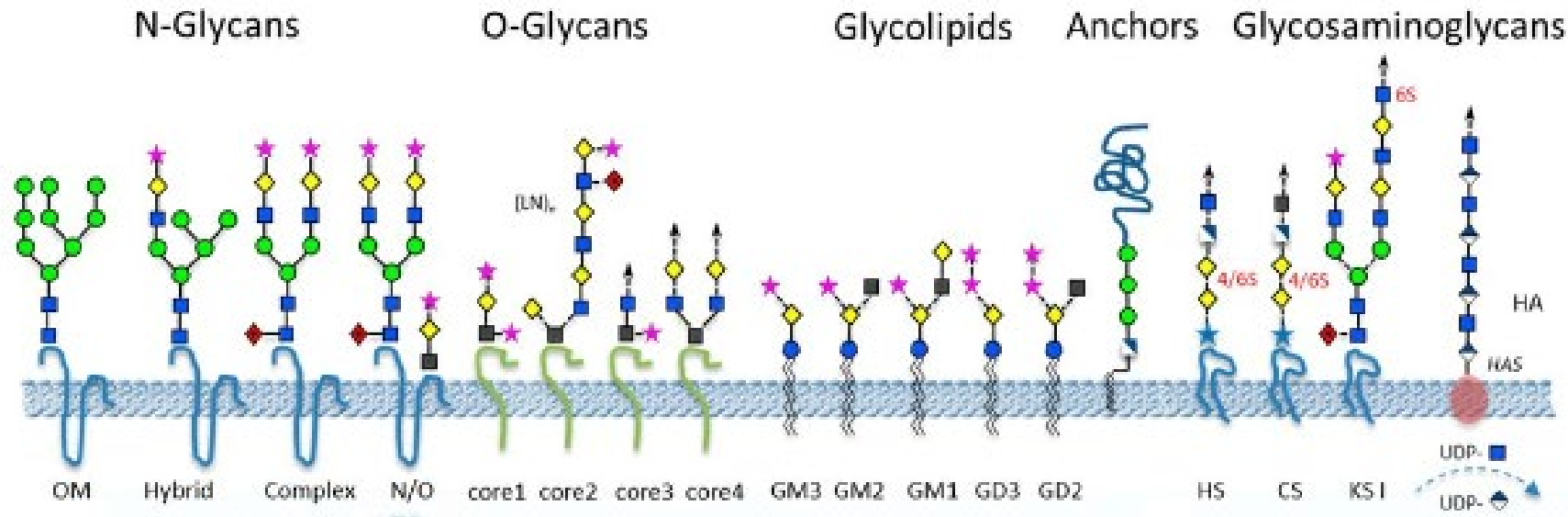
Office of Strategic Coordination – The Common Fund

Glycoscience

Glycans:

Information rich, structurally diverse, can themselves be modified, & play key roles in nearly every aspect of human biology and disease.

Major classes of glycan



Science 03 Jan 2014:
Vol. 343, Issue 6166, 1235681

Pragmatic Issues in Glycoscience

Glycoscience a highly specialized field

- Many technical challenges
- Not enough experts to help newcomers

Specialized Expertise, Methods, Instruments

- Cost of capital equipment (NMR, MS)
- Dedicated personnel
- Access

Ambiguity in structure determination

- Glycan microheterogeneity
- Branching
- Isomeric monosaccharides
- Linkage positions, stereochemistry

Lack of:

- Ready access to synthetic oligosaccharides
- Analytical and Computational Tools
- Databases
- High throughput platforms
- Training for non-specialists



The Glycoscience Traffic Jam

2012 Transforming Glycoscience: A Roadmap for the Future

In 2012, NIH commissioned a NASEM study on the field of Glycoscience.

Committee on Assessing the Importance & Impact of Glycomics & Glycosciences
National Research Council, National Academy of Science

The Study Noted:

- *Glycans play central roles in most biological processes*
- *Understudied due to a lack of tools to probe their often-complex structures and properties.*

Identified Priorities:

*A roadmap for transforming glycoscience **from a field dominated by specialists to a widely studied and integrated discipline**, which could lead to a more complete understanding of glycans and help solve key challenges in diverse fields.*

This led to development of the NIH Common Fund Glycoscience program.

<https://nap.nationalacademies.org/catalog/13446/transforming-glycoscience-a-roadmap-for-the-future>

NIH Common Fund Glycoscience Program

Goal: Create accessible methods and resources to study glycans for use by the broader biomedical research community.

Total Investment: \$111M over 7 years

Initiative 1: Facile methods and technologies for synthesis of biomedically relevant glycans (\$38M)

Initiative 2: Accessible analytical tools for structure determination and functional assays (\$55M)

Initiative 3: Informatics tools for data integration and analysis (\$10M)

Initiative 4: Supplements to non-specialists to support early adoption of program resources (\$5.7M)

Activity Code	# Awards	FY15	FY16	FY17	FY18	FY19	FY20	FY21
Synthesis								
U01	6							
	6							
	6							
Tools								
R21	13							
	17							
U01	2							
	3							
	9							
	8							
	7							
Informatics								
R34	2							
U01	1							
Supplements for Early Adoption								
Supplement	7							
Supplement	11							

Common Fund Glycoscience Working Group

Co-Chairs

Jon Lorsch, Director, NIGMS

Martha Somerman, Director, NIDCR

OSC Trio Staff

Ananda Roy

Jessica Smith

Tony Casco

Brionna Hair

Program Coordinators/Project Leaders

Pamela Marino, NIGMS

Douglas Sheeley, NIGMS (NIDCR, OSC)

Karl Krueger, NCI

Amanda Melillo, NIDCR (NIGMS, NIDCR)

Preethi Chander NIDCR

Working Group Members

Rita Sarkar, NHLBI

Austin Yang, NIA

Amy Krafft, NIAID

Mercy Prabhudas, NIAID

Daniel Raiten, NICHD

Dona Love, NIAID

Austin Yang, NIA

Salvatore Sechi, NIDDK

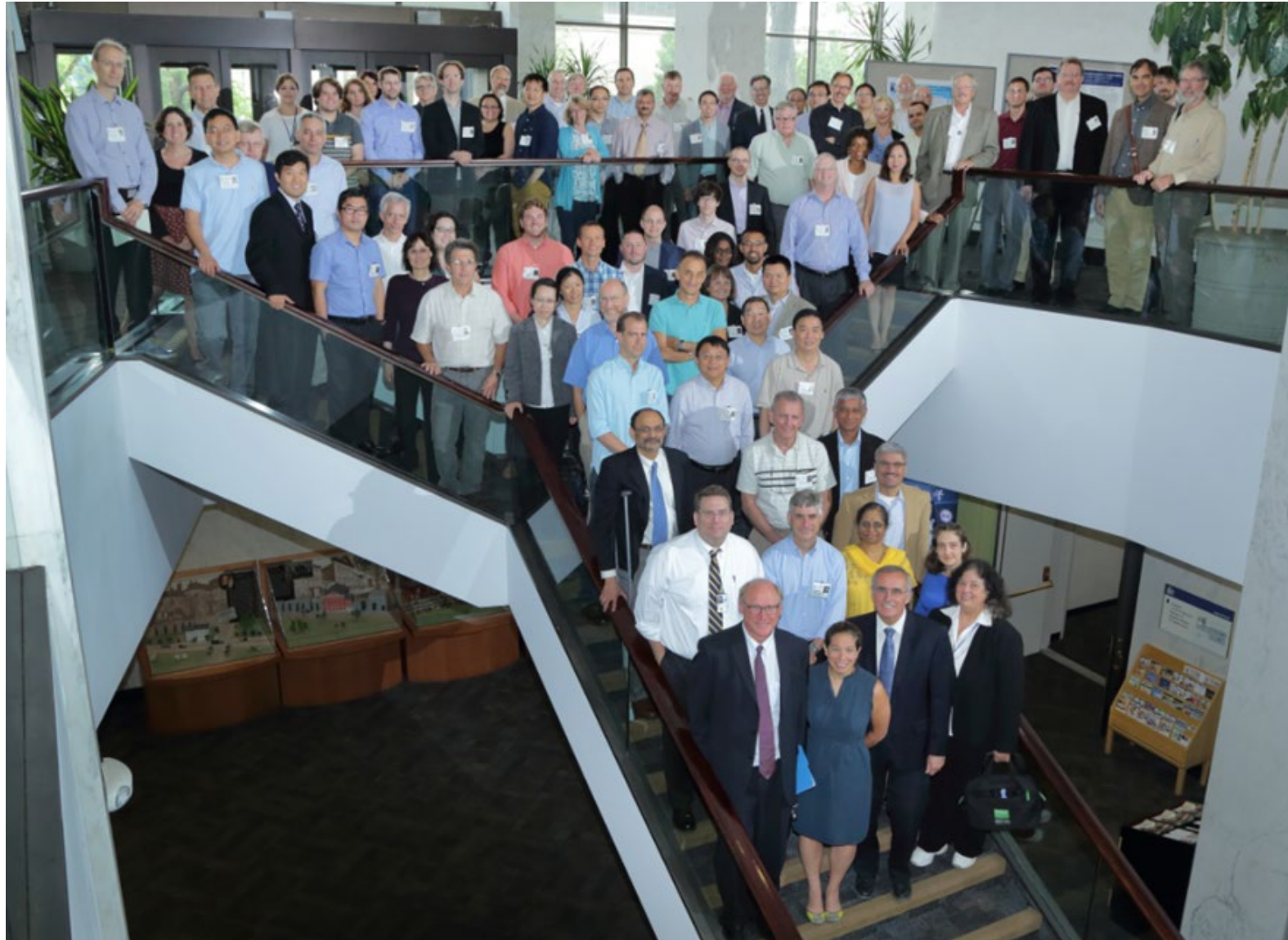
Houman Araj, NEI

Angela Malaspina, NIAID

Rao Rapaka, NIDA

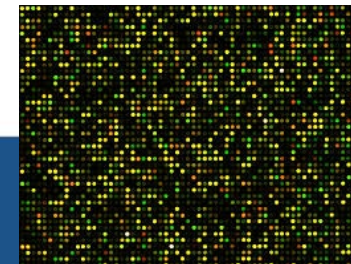
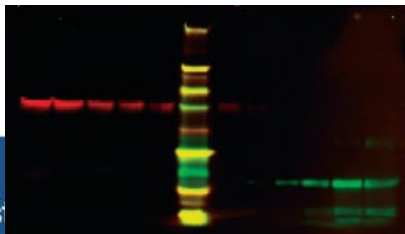
Tony Kirilusha, NIAMS

Kiran Vemuri, NIDA



The Glycoscience Program Created an Accessible “Glyco Toolbox”

- New catalytic & chemoenzymatic methods for the synthesis of glycans/ glycan libraries are in place.
- Automation platforms that can be easily adapted by Cores are available.
- Analysis, labeling, and modeling tools/technologies with demonstrated proof-of-concept and public health relevance are being commercialized.
- A unified informatics effort is moving forward to integrate glycoscience with other molecular databases.
- The Human GlycoEnzymes are commercially available.



Computational and informatics resources and tools for glycosciences research

- Training Resources
- Integration with protein and glycan databases worldwide
- **Quick Search:** Multi-domain queries based on user requests
- **Super Search:** GUI to build queries across all GlyGen datasets

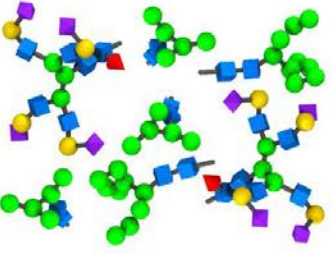


GlyGen: Computational and Informatics Resources for Glycoscience
 GlyGen is a data integration and dissemination project for carbohydrate and glycoconjugate related data. GlyGen retrieves information from multiple international data sources and integrates and harmonizes this data. This web portal allows exploring this data and performing unique searches that cannot be executed in any of the integrated databases alone.

HOME EXPLORE QUICK SEARCH TRY ME DATA TOOLS HELP ABOUT

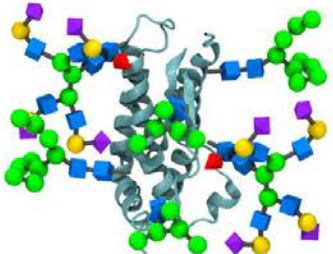
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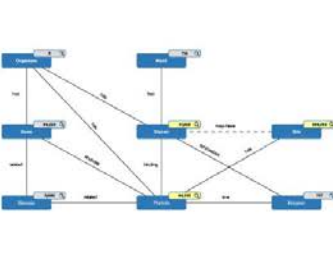
Glycan Search
 Search for glycan structures based on their chemical and structural properties.

EXPLORE



Protein Search
 Search for proteins based on their sequences, accessions, and annotations.

EXPLORE



Super Search
 Super search is a graphical interface to build queries across all GlyGen datasets.

EXPLORE

Version
 Portal: 2.2 (02/Oct/2023)
 Webservice: 2.2 (02/Oct/2023)
 Data: 2.2.1 (02/Oct/2023)


Featured Video



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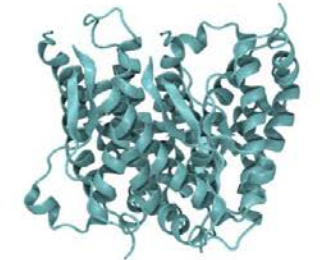
Database Statistics

Species	Glycans	Proteins	Glycoproteins
Human	20258	20586	11623
Rat	7860	22870	2680
Mouse	7501	21837	7307
SARS-CoV-2	1116	17	4
Yeast	1101	6060	883
Fruit fly	884	13821	781
HCoV-SARS	21	15	3
HCV-H			



Quick Search
 Quick Search provides multi-domain queries that are based on user requests.

EXPLORE



Site Search
 Search for proteins based on their site and site annotations.

EXPLORE



GlyGen Mapper
 ID mapping related to glycan, protein / glycoprotein and based on the user input.

EXPLORE

U01 GM125267 → R24 GM146616

<http://www.glygen.org>



glygen.org/protein_list.html?id=3bae114e248fc8fb929bb8ecfe482e40

GlyGen HOME EXPLORE QUICK SEARCH TRY ME DATA HELP MORE Search.. Beta Testing MY GLYGEN

Protein Search / Protein List

Summary of your Protein Search

Performed on: January 23rd 2020, 2:59:57 pm (EST)

Search Term:

Search Category:

** To perform the same search again using the current version of the database, click "Update Results".

Page Records per page "15 Proteins were found" [DOWNLOAD](#)

UniProtKB Accession	Gene Name	UniProtKB Name	Chemical Mass (Da)	Organism	RefSeq Name	RefSeq Accession
P0DN86-1	CGB3	Choriogonadotropin subunit beta 3	17739	Homo sapiens	choriogonadotropin subunit beta 3 precursor	NP_000728.1
P00000-1	LHCGR	Lutropin-choriogonadotropic hormone receptor	78643	Homo sapiens	lutropin-choriogonadotropic hormone receptor precursor	NP_000224.2
P01215-1	CGA	Glycoprotein hormones alpha chain	13075	Homo sapiens	glycoprotein hormones alpha chain isoform 1 precursor	NP_001239312.1
P16255-1	Lhcgr	Lutropin-choriogonadotropic hormone receptor	78036	Rattus norvegicus	lutropin-choriogonadotropic hormone receptor precursor	NP_037110.1
P0DN87-1	CGB7	Choriogonadotropin subunit beta 7	17757	Homo sapiens	choriogonadotropin subunit beta 7 precursor	NP_149133.1
O60927-1	PPP1R11	E3 ubiquitin-protein ligase PPP1R11	13953	Homo sapiens	E3 ubiquitin-protein ligase PPP1R11	NP_068778.1
Q6NT52-1	CGB2	Choriogonadotropin subunit beta variant 2	17374	Homo sapiens	choriogonadotropin subunit beta variant 2 isoform 1 precursor	NP_203696.2
A6NKQ9-1	CGB1	Choriogonadotropin subunit beta variant 1	20468	Homo sapiens	choriogonadotropin subunit beta variant 1 precursor	NP_203695.2
Q9Z2M6-1	Ubl3	Ubiquitin-like protein 3	13180	Mus musculus	ubiquitin-like protein 3 isoform a precursor	NP_036038.1
O95164-1	UBL3	Ubiquitin-like protein 3	13157	Homo sapiens	ubiquitin-like protein 3 precursor	NP_009037.1
Q6UX06-1	OLFM4	Olfactomedin-4	57280	Homo sapiens	olfactomedin-4 precursor	NP_006409.3
Q9R005-1	Pr17d1		27821	Rattus norvegicus	prolactin-7D1 precursor	NP_445816.1
Q3T1J1-1	Eif5a	Eukaryotic translation initiation factor 5A-1	16832	Rattus norvegicus	eukaryotic translation initiation factor 5A-1	NP_001028853.1
Q61184-1	Mtnr1a	Melatonin receptor type 1A	39837	Mus musculus	melatonin receptor type 1A	NP_032665.1
P17256-1	Mvk	Mevalonate kinase	41988	Rattus norvegicus	mevalonate kinase	NP_112325.1

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Funded by NIH Glycoscience Common Fund
Grant # 1U01GM125267 - 01

glygen.org/protein_detail.html?uniprot_canonical_ac=P01215-1&listID=3bae114e248f8fb929bb8ecfe482e40&gs=

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Protein Search / Protein List / Protein Detail

Details for protein P01215-1

DOWNLOAD

General

Species

Function

GO Annotation

Glycosylation

Sequence

Pathway

Isoforms

Homologs

Disease

Mutation

Expression Tissue

Expression Disease

Cross References

Publications

General

- Gene Name: [CGA](#)
- Gene Location: Chromosome: 6 (87,095,406 - 87,085,498)
- [Ensembl Gene](#)
- UniProtKB ID: [GLHA_HUMAN](#)
- UniProtKB Accession: [P01215-1](#)
- UniProtKB Accession Length: 116
- UniProtKB Entry Name: Glycoprotein hormones alpha chain
- Chemical Mass: 13,075 Da
- RefSeq Accession: [NP_001239312.1](#)
- RefSeq Name: glycoprotein hormones alpha chain isoform 1 precursor
- RefSeq Summary: The four human glycoprotein hormones chorionic gonadotropin (CG), luteinizing hormone (LH), follicle stimulating hormone (FSH), and thyroid stimulating hormone (TSH) are dimers consisting of alpha and beta subunits that are associated noncovalently. The alpha subunits of these hormones are identical, however, their beta chains are unique and confer biological specificity. The protein encoded by this gene is the alpha subunit and belongs to the glycoprotein hormones alpha chain family. Two transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Nov 2011].

Species

- Homo sapiens [UniProtKB](#)
- Taxonomy ID: 9606

Function

Shared alpha chain of the active heterodimeric glycoprotein hormones thyrotropin/thyroid stimulating hormone/TSH, lutropin/luteinizing hormone/LH, follitropin/follicle stimulating hormone/FSH and chorionogonadotropin/CG. These hormones bind specific receptors on target cells that in turn activate downstream signaling pathways. [UniProtKB](#)

GDF9 promoted follicle-stimulating hormone (FSH)-induced progesterone production and STAR expression.

These results suggested that the melatonin receptors MTNR1A and MTNR1B are essential to repress hCG-induced endoplasmic reticulum stress and cell apoptosis. Publication Status: Online-Only

The present results clearly demonstrated that NF-kappaB was activated to regulate VEGF expression by increasing HIF-1alpha transcription in luteal cells treated with HCG. [RefSeq](#)

Sex, age, season, and sampling time significantly affected serum TSH concentrations.

The measured hCG values are considerably different depending on the pregnancy result, which is why this value is considered

Feedback

Protein Search / Protein List / Protein Detail

Details for protein P01215-1

General

- Gene Name: **CGA**
- Gene Location: Chromosome: 6 (87,095,406 - 87,085,498)
[Ensembl Gene](#)
- UniProtKB ID: **GLHA_HUMAN**
- UniProtKB Accession: **P01215-1**
- UniProtKB Accession Length: **116**
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UniProtKB **RefSeq**

The screenshot displays the UniProtKB entry for P01215 (GLHA_HUMAN). The interface includes a navigation sidebar on the left with categories like General, Species, Function, GO Annotation, Glycosylation, Sequence, Pathway, Isoforms, Homologs, Disease, Mutation, Expression Tissue, Expression Disease, Cross References, and Publications. The main content area shows the protein name, gene symbol (CGA), and organism (Homo sapiens). The 'Function' section describes the shared alpha chain of various hormones. The 'GO' section lists molecular functions like hormone activity and biological processes like signaling pathways. The 'Keywords' section includes 'Hormone'. The 'Enzyme and pathway databases' section lists various identifiers and their corresponding pathways. The 'Names & Taxonomy' section provides the recommended name and alternative names.

UniProtKB - P01215 (GLHA_HUMAN)

Entry | Protein | **Glycoprotein hormones alpha chain**

Gene | **CGA**

Organism | *Homo sapiens (Human)*

Status | Reviewed - Annotation score: ●●●●● - Experimental evidence at protein levelⁱ

Functionⁱ

Shared alpha chain of the active heterodimeric glycoprotein hormones thyrotropin/thyroid stimulating hormone/TSH, lutropin/luteinizing hormone/LH, follitropin/follicle stimulating hormone/FSH and choriogonadotropin/CG. These hormones bind specific receptors on target cells that in turn activate downstream signaling pathways. [2 Publications](#)

GO - Molecular functionⁱ

- follicle-stimulating hormone activity [Source: UniProtKB](#)
- hormone activity [Source: AgBase](#)

Complete GO annotation on QuickGO ...

GO - Biological processⁱ

- G protein-coupled receptor signaling pathway [Source: UniProtKB](#)
- peptide hormone processing [Source: Reactome](#)
- positive regulation of cell migration [Source: BHF-UCL](#)
- positive regulation of cell population proliferation [Source: BHF-UCL](#)
- positive regulation of steroid biosynthetic process [Source: UniProtKB](#)
- positive regulation of transcription by RNA polymerase II [Source: BHF-UCL](#)
- regulation of signaling receptor activity [Source: UniProtKB](#)
- regulation of transcription by RNA polymerase II [Source: Reactome](#)
- thyroid hormone generation [Source: GO_Central](#)

Complete GO annotation on QuickGO ...

Keywordsⁱ

Molecular function	Hormone
--------------------	---------

Enzyme and pathway databases

Reactome ⁱ	R-HSA-193048 Androgen biosynthesis R-HSA-193993 Mineralocorticoid biosynthesis R-HSA-209822 Glycoprotein hormones R-HSA-209968 Thyroxine biosynthesis R-HSA-375281 Hormone ligand-binding receptors R-HSA-418555 G alpha (s) signalling events R-HSA-8866910 TRAP2 (AP-2) family regulates transcription of growth factors and their receptors R-HSA-975578 Reactions specific to the complex N-glycan synthesis pathway
SABIO-RK ⁱ	P01215
SIGNOR ⁱ	P01215

Names & Taxonomyⁱ

Protein names ⁱ	Recommended name: Glycoprotein hormones alpha chain Alternative name(s): • Anterior pituitary glycoprotein hormones common subunit alpha
----------------------------	--

glygen.org/protein_detail.html?uniprot_canonical_ac=P01215-1&listID=3bae114e248fc8fb929bb8ecfe482e40&gs=

General

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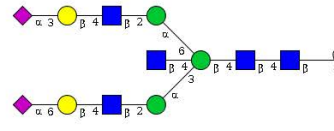
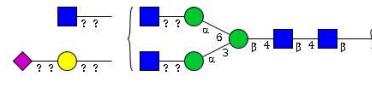
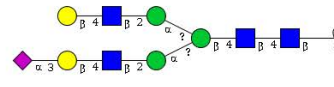
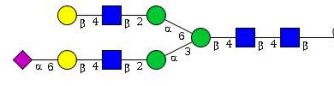
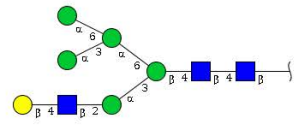
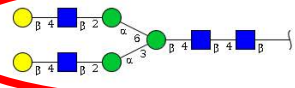

Expression Disease

Cross References

Publications

Glycosylation

With Reported Glycans Without Reported Glycans

Sources	GlyYouCan Accession	Type	Residue	Image of Glycan Structure
UniCarbKB 1 PubMed 4	G14998UC	N-linked	Asn76	
UniCarbKB 1 PubMed 1	G55504WE	N-linked	Asn76	
UniCarbKB 1 PubMed 4	G93284HQ	N-linked	Asn76	
UniCarbKB 1 PubMed 4	G91365ZQ	N-linked	Asn76	
UniCarbKB 1 PubMed 4	G16828VN	N-linked	Asn76	
UniCarbKB 1 PubMed 4	G36191CD	N-linked	Asn76	
UniCarbKB 1	G69411IG	N-linked	Asn76	

UniCarbKB	PubMed	Glycan Type	Asn76	Structure
G99897FQ	1991473	N-linked	Asn76	
G42358LZ		N-linked	Asn76	
G06209KS		N-linked	Asn76	

Showing 1 to 10 of 83 rows rows per page

Glycan structures accurately reflected in PDB

3D Structure viewing with "ball and stick" landmarks for glycans

3D View: 1HD4

UniCarbKB 1
P01215

PubMed 4
9449027
1991473
8026573
1820200

UniCarbKB 1
G42358LZ

PubMed 1

UniCarbKB 1
G06209KS

PubMed 4

Showing 1 to 10 of 83 rows 10 rows per page

Glycan Details | Details for G99897FQ

Details For Glycan G99897FQ

General

3D View

Organism

Names

Motifs

Associated Protein

Source	Protein Name	UniProtKB Accession	Position	Organism
UniCarbKB	Glycoprotein hormone alpha chain	P01215-1	Asn78	Homo sapiens
UniCarbKB	Glycoprotein hormone alpha chain	P01215-1	Asn102	Homo sapiens
UniCarbKB	Luteinizing hormone subunit beta	P01225-1	Asn50	Homo sapiens

accurately
glycan
landmarks

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Eur J Biochem. 1991 Jan 1; 195(1):257-68.

NMR investigations of the N-linked oligosaccharides at individual glycosylation sites of human lutropin.

Weisshaar G¹, Hiyama J, Renwick AG, Nimtz M

Author information


Abstract
 Human lutropin or luteinizing hormone (hLH) is a heterodimeric glycoprotein, composed of two subunits. hLH alpha (N-glycosylated at Asn52 and Asn78) and hLH beta (N-glycosylated at Asn30). The sugar chains were liberated by hydrazinolysis from intact hLH beta and from glycopeptides obtained after tryptic digestion of hLH alpha, subsequently reduced and fractionated as aldolols by anion-exchange and ion-suppression amine-adsorption HPLC and identified mainly by one-dimensional (1D) and two-dimensional (2D) 1H-NMR spectroscopy. The results indicate predominantly diantennary, N-acetyllactosamine-type structures at all three glycosylation sites. The oligosaccharides attached to Asn52 (hLH alpha) and Asn30 (hLH beta) show a remarkably similar pattern, with mainly chain-terminating 4-sulphated 2-deoxy-2-N-acetylamino-D-galactose (GalNAc) and a sulphated/sialylated structure as the major single component. However, virtually all N-glycans on the beta subunit bear a fucose residue alpha 1-6-linked to the proximal GlcNAc, whereas those at Asn52 (and Asn78) of the alpha subunit are predominantly non-fucosylated. The oligosaccharides at Asn78 (hLH alpha) are sialylated rather than sulphated and contain the unique sequence NeuAc alpha 2-6 GalNAc beta 1-4GlcNAc beta 1-2 Man alpha 1-3 as part of the majority of mono- and disialylated compounds. The major single constituent at Asn78 has the following structure: [formula, see text].

PMID: 1991473 DOI: [10.1111/j.1432-1033.1991.tb15702.x](https://doi.org/10.1111/j.1432-1033.1991.tb15702.x)


[Indexed for MEDLINE] [Free full text](#)



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The asparagine-linked oligosaccharides at individual glycosylation sites [Glycobiology. 1992]

Site-specific N-glycosylation of human chorionic gonadotrophin--structural an [Glycobiology. 1991]

Review Pituitary glycoprotein hormone oligosaccharides. st [Biochim Biophys Acta. 1988]

Review In vivo targeting function of N-linked oligosaccharides. Pharr [Adv Exp Med Biol. 1995]

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[See all...](#)

Cited by 18 PubMed Central articles

Review Follicle-Stimulating Hormone Glycobiology. [Endocrinology. 2019]

Low-glycosylated forms of both FSH and LH play major roles in the natural o [Ups J Med Sci. 2018]

Review *In Vivo* and *In Vitro* Impact of Carbohydrate [Front Endocrinol (Lausanne). 2...]

[See all...](#)

Related information

Gene

HomoloGene

Nucleotide

Nucleotide (RefSeq)

Nucleotide (Weighted)

Protein (RefSeq)

Protein (Weighted)

PubChem Compound (MeSH Keyword)

Taxonomy via GenBank

UniGene

Publication type, MeSH terms, Substances +

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Format: Abstract

Eur J Biochem. 1991 Jan 1; 195(1):257-68.

NMR investigations of the N-linked oligosaccharides at individual glycosylation sites of lutropin.

Weisshaar G¹, Hiyama J, Renwick AG, Nimtz M

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Abstract

Human lutropin or luteinizing hormone (hLH) is a heterodimeric glycoprotein, composed of two subunits. hLH alpha (N-glycosylated at Asn78) and hLH beta (N-glycosylated at Asn30). The sugar chains were liberated by hydrazinolysis from intact hLH and from glycopeptides obtained after tryptic digestion of hLH alpha, subsequently reduced and fractionated as aldolites by anion-suppression amine-adsorption HPLC and identified mainly by one-dimensional (1D) and two-dimensional (2D) ¹H-NMR results indicate predominantly diantennary, N-acetyllactosamine-type structures at all three glycosylation sites. The oligosaccharides attached to Asn52 (hLH alpha) and Asn30 (hLH beta) show a remarkably similar pattern, with mainly chain-terminating 4-sulphated acetylaminosaccharides (GalNAc) and a sulphated/sialylated structure as the major single component. However, virtually all N-glycans on the beta subunit bear a fucose residue alpha 1-6-linked to the proximal GlcNAc, whereas those at Asn52 (and Asn78) of predominantly non-fucosylated. The oligosaccharides at Asn78 (hLH alpha) are sialylated rather than sulphated and contain the unique sequence NeuAc alpha 2-6 GalNAc beta 1-4 GlcNAc beta 1-2 Man alpha 1-3 as part of the majority of mono- and disialylated compounds. The major single constituent at Asn78 has the following structure: [formula, see text].

PMID: 1991473 DOI: [10.1111/j.1432-1033.1991.tb15702.x](https://doi.org/10.1111/j.1432-1033.1991.tb15702.x)

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Publication type, MeSH terms, Substances

LinkOut - more resources

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NMR investigations of the N-linked oligosaccharides at individual glycosylation sites of human lutropin

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Human lutropin or luteinizing hormone (hLH) is a heterodimeric glycoprotein, composed of two subunits, hLH α (N-glycosylated at Asn52 and Asn78) and hLH β (N-glycosylated at Asn30). The sugar chains were liberated by hydrazinolysis from intact hLH and from glycopeptides obtained after tryptic digestion of hLH, subsequently reduced and fractionated as aldolites by anion-suppression amine-adsorption HPLC and identified mainly by one-dimensional (1D) and two-dimensional (2D) ¹H-NMR spectroscopy. The results indicate predominantly diantennary, N-acetyllactosamine-type structures at all three glycosylation sites. The oligosaccharides attached to Asn52 (hLH α) and Asn30 (hLH β) show a remarkably similar pattern, with mainly chain-terminating 4-sulphated 2-deoxy-2-N-acetylaminosaccharides (GalNAc) and a sulphated/sialylated structure as the major single component. However, virtually all N-glycans on the β subunit bear a fucose residue α 1-6-linked to the proximal GlcNAc, whereas those at Asn52 (and Asn78) of the α subunit are predominantly non-fucosylated. The oligosaccharides at Asn78 (hLH α) are sialylated rather than sulphated and contain the unique sequence NeuAc α 2-6GalNAc β 1-4GlcNAc β 1-2Man α 1-3 as part of the majority of mono- and disialylated compounds. The major single constituent at Asn78 has the following structure:

NeuAc α 2-3Gal β 1-4GlcNAc β 1-2Man α 1-6
Man β 1-4GlcNAc β 1-4GlcNAc-ol.

NeuAc α 2-6GalNAc β 1-4GlcNAc β 1-2Man α 1-3

hLH is a heterodimeric glycoprotein hormone that consists of two non-covalently associated subunits, both highly cross-linked by disulphide bonds: the α subunit (hLH α) bears N-glycans at positions Asn52 and Asn78, the β subunit (hLH β) is N-glycosylated at Asn30. The hormone, which is a vital component of the reproductive process, is produced in the anterior pituitary gland and stimulates steroidogenesis in ovary and testis [1–3]. The α subunit shares an identical amino acid sequence and carbohydrate attachment sites with the respective α subunits of human follicle-stimulating hormone (follicle-stimulating hormone) and thyrotropin (thyroid-stimulating hormone), produced in the same gland, and with that of human chorionic gonadotropin from the placenta; the four closely related hormones differ structurally from each other with regard to their hormone-specific β subunits and the carbohydrate structures attached to both subunits [3–7]. Numerous investigations, mostly on human chorionic gonadotropin, suggest that the sugar chains are not required for hormone-receptor binding, but play a critical role in receptor activation via the adenylate-cyclase enzyme system [2, 3, 8–10 (and the references cited therein)]. More recently, subunit- and site-specific functions of the carbohydrate moieties have been reported, and the sugar chains on the α subunits, primarily at Asn52, have been found to be more important with respect to hormone assembly, secretion and signal transduction [10–13]. Detailed studies of the acidic oligosaccharides in pituitary glycoprotein hormones from three different species [4–6] demonstrated that the carbohydrate structures of hLH comprise a highly heterogeneous mixture of almost exclusively diantennary N-acetyllactosamine-type N-glycans with the peripheral sequences NeuAc α 2-3/6Gal and/or SO₄-4GalNAc; the latter has so far only been found in pituitary glycoproteins (note that the term N-acetyllactosamine-type is used throughout the text according to IUPAC nomenclature, although most N-glycans described contain the sequence GalNAc β 1-4GlcNAc rather than Gal β 1-4GlcNAc).

For a better assessment of the roles played by carbohydrates in biosynthesis and function of these glycoprotein hormones, knowledge of the detailed oligosaccharide structures at individual glycosylation sites is required. We have recently reported on the distinct site-specific glycosylation of

Correspondence to A. G. C. Renwick, Department of Biochemistry, University of Auckland, Private Bag, Auckland, New Zealand.

Abbreviations: COSY, scalar shift-correlated NMR spectroscopy; 1D, one-dimensional; 2D, two-dimensional; FAB-MS, fast-atom-bombardment mass spectrometry; Fuc, L-fucose; GalNAc, 2-deoxy-2-N-acetylaminosaccharide; GlcNAc-ol, N-acetylglucosamine; hLH, human lutropin; hLH α , α subunit of hLH; hLH β , β subunit of hLH.

Enzyme. Trypsin (EC 3.4.21.4).

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Eur J Biochem. 1991 Jan 1; 195(1):257-68.

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Weisshaar G¹, Hiyama J, Renwick AG, Nimtz M

Author information

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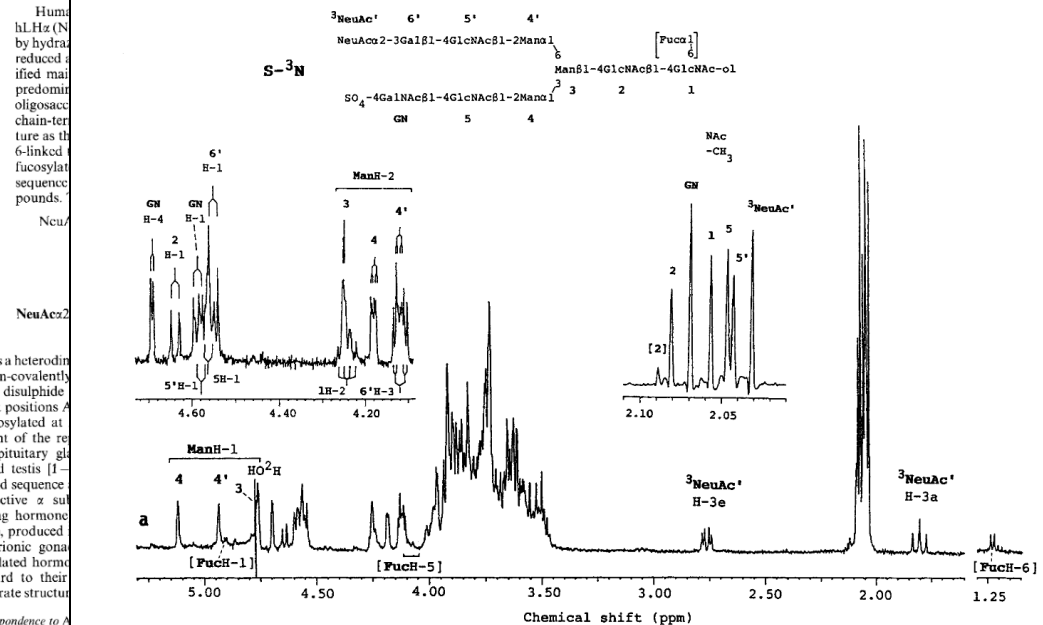
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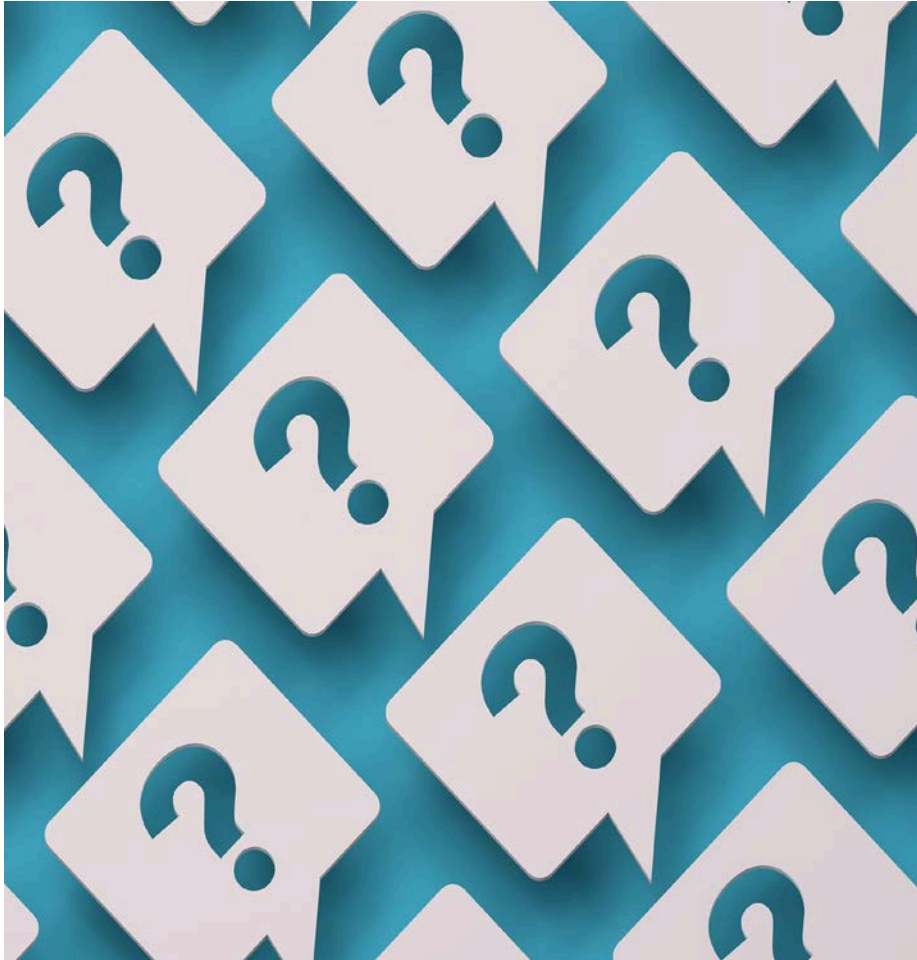
hLH is a heterodimer of two non-covalently linked by disulphide glycosylated at positions Asn78 is N-glycosylated at the component of the anterior pituitary gland ovary and testis [1-stimulating hormone (hormone), produced by the human chorionic gonadotropin with regard to their carbohydrate structure.

Correspondence to Prof. G. Weisshaar, University of Auckland, Department of Biochemistry, Private Bag 920, Auckland, New Zealand.
Abbreviations: COSY, 1D, one-dimensional; 2D, two-dimensional; MS, mass spectrometry; 2-N, 2-N-acetyllactosamine; hLH, human lutropin; hLH, human lutropin; E, enzyme; Trypsin (E, trypsin).

Fig. 4. 400-MHz ¹H-NMR spectrum of fraction A_{1-4c} recorded in ²H₂O at 298 K. Labelling of sugar residues refers to structure on top of the figure; assignments in square brackets correspond to the minor fucosylated compound (15%). (a) Resolution-enhanced 1D ¹H-NMR spectrum; NAc signals and the spectral region of 4.08 – 4.73 ppm are expanded and the resolution enhanced further. (b) 2D COSY spectrum; 4H1, 4'H1, etc. denote diagonal peaks of Man4 H-1, Man4' H-1, etc.; 4H1/H2, 4'H1/H2, etc. denote cross peaks between Man4 H-1 and H-2, Man4' H-1 and H-2, etc. The cross peak between Man3 H-1 and H-2 is missing in the spectrum due to the small coupling constant J_{1,2} (< 1 Hz) and a short effective transverse relaxation time T₂* ([31]) and the references cited therein

Glycoscience Program Evaluation

Evaluation Questions



Key Questions

1. What new resources for the glycosciences were developed by the program and how were these resources made available to the community?
2. How and to what extent are glycoscientists and non-glycoscientists using resources developed by the Glycoscience Program?
3. How has the program facilitated access to resources for the glycosciences?

Evaluation Implementation

- The NIH Office of the Director (OD) requested a summative evaluation of the Glycoscience Program (GSP).
- Ripple Effect worked with the OD and the PP&E Branch to design and implement an evaluation to assess the extent to which the GSP achieved its goals.

Evaluation Methods



Bibliometric Analysis

- GSP catalog of awards and resources
- Publication and bibliometric data
- Corresponding author glycoscientist classification analysis



Qualitative Data

- 20 in-depth interviews
 - Glycoscientists (n=5)
 - Non-specialists (n=15)

Q1. What new resources for the glycosciences were developed by the GSP and how were they made available to the community?



National Institutes of Health

Office of Strategic Coordination – The Common Fund

GSP Resources Developed

GSP Resources Dissemination Stratified by the GSP Initiatives

Characteristics	Overall	Synthesis	Tools	Informatics
GSP Resources	56	18	37	1
GSP-Resource Publications	153	81	71	2
Resources with publications	49 (88%)	18 (100%)	30 (81%)	1 (100%)
Publications per resource (range)	0-11	2-11	0-5	n/a
Publications per resource (average)	2.7	4.6	1.9	n/a
Resources with website(s)	21 (38%)	4 (22%)	16 (43%)	1 (100%)
Unique websites	25	5	19	1
Resources with commercialization	15 (27%)	7 (39%)	8 (22%)	0

GSP Resources - Dissemination

How participants learned about GSP and GSP resources

Findings	NS	G
Connections with collaborators and colleagues	12	3
Conferences and meetings	9	4
NIH dissemination	8	3
Webinars and workshops	8	1
Publications	3	3
GSP Website	6	0

Non-specialist n=15, Glycoscientist n=5

Q2. How and to what extent are glycoscientists and non-specialists using resources developed by the GSP?

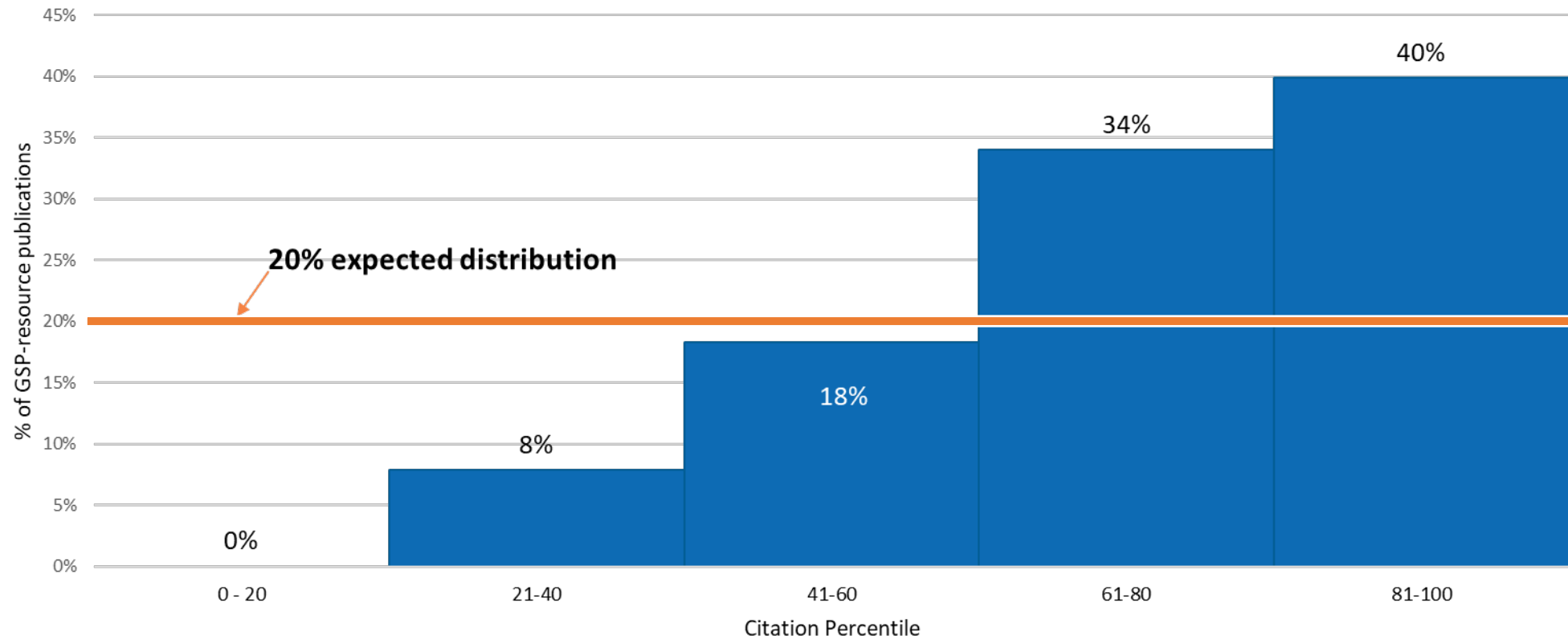
Citation of GSP Resources

GSP-Resource Citation Metrics by GSP Initiative

Citation Metrics	Overall (n=153)	Synthesis (n=81)	Tools (n=71)	Informatics (n=2)
Total citations	4,361	2,041	2,248	81
Average citations per GSP-resource publication	29	25	32	41
Total citations (self-citations removed)	3,553	1,690	1,816	53
% self-citations	19%	17%	9%	35%
Unique citing publications	2,813	1,232	1,616	66
RCR (median)	1.4	1.2	1.7	4.9
Citation percentile (average)	72	70	73	88
Average citation lag (days)	204	224	206	123

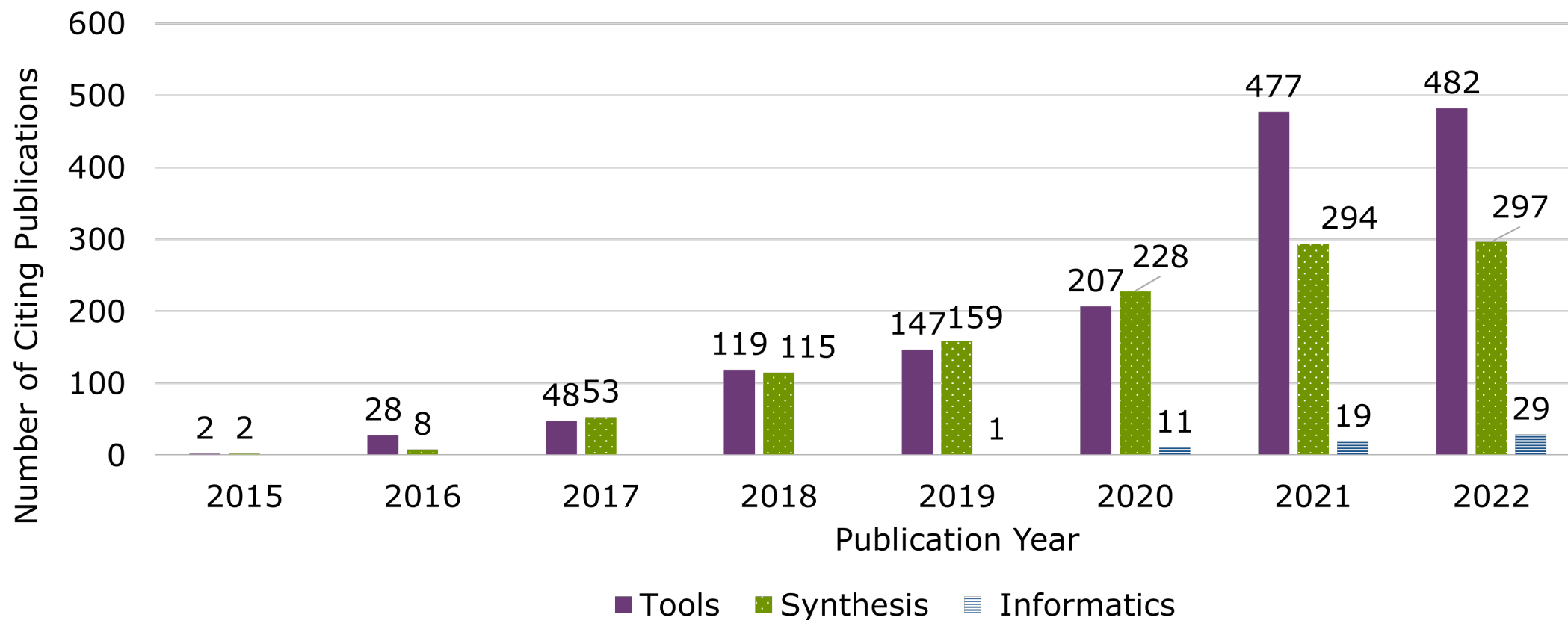
Citation of GSP Resources

GSP-Resource Publications by Citation Percentile

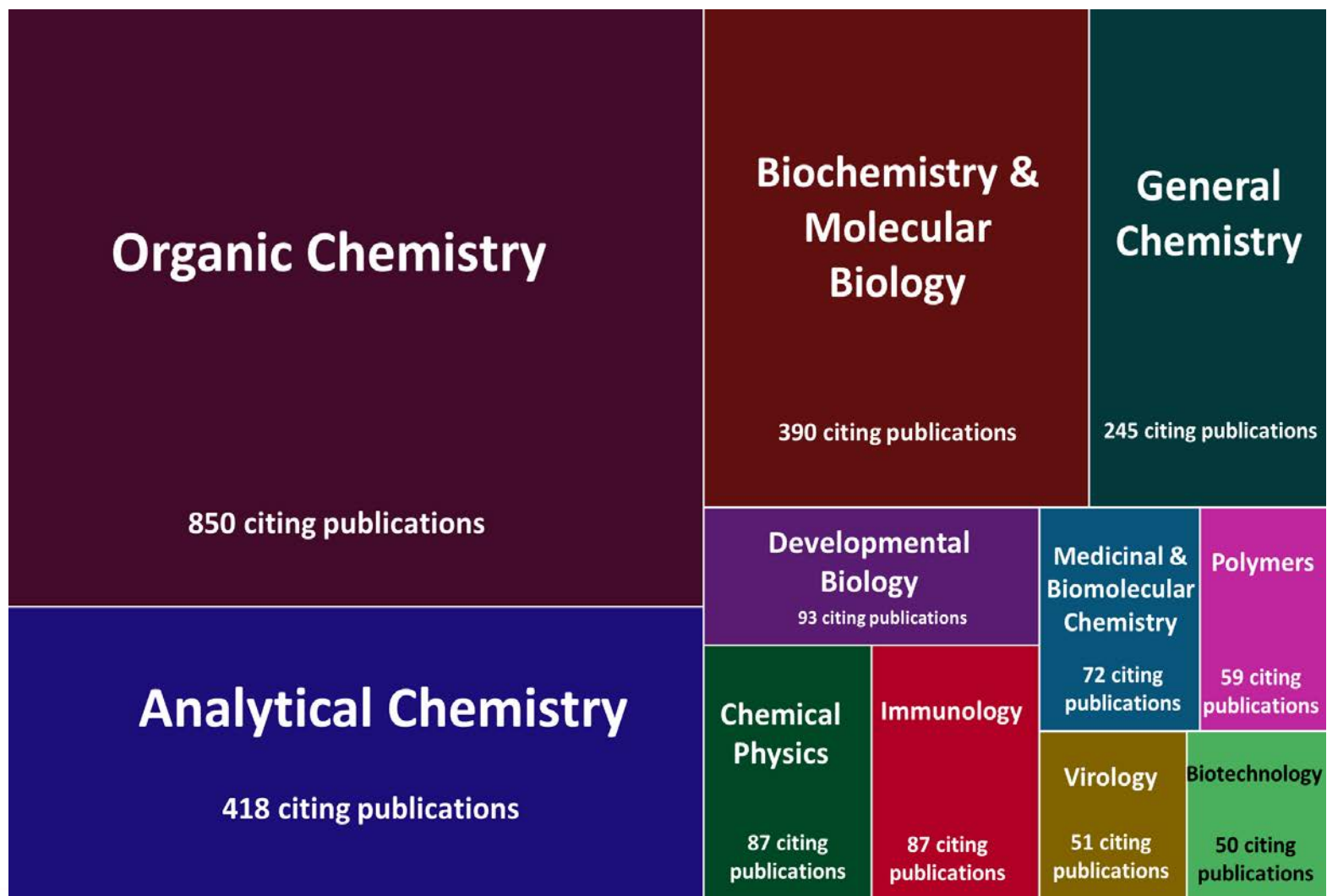


Citation of GSP Resources

Distribution of Citing Publications by Publication Year



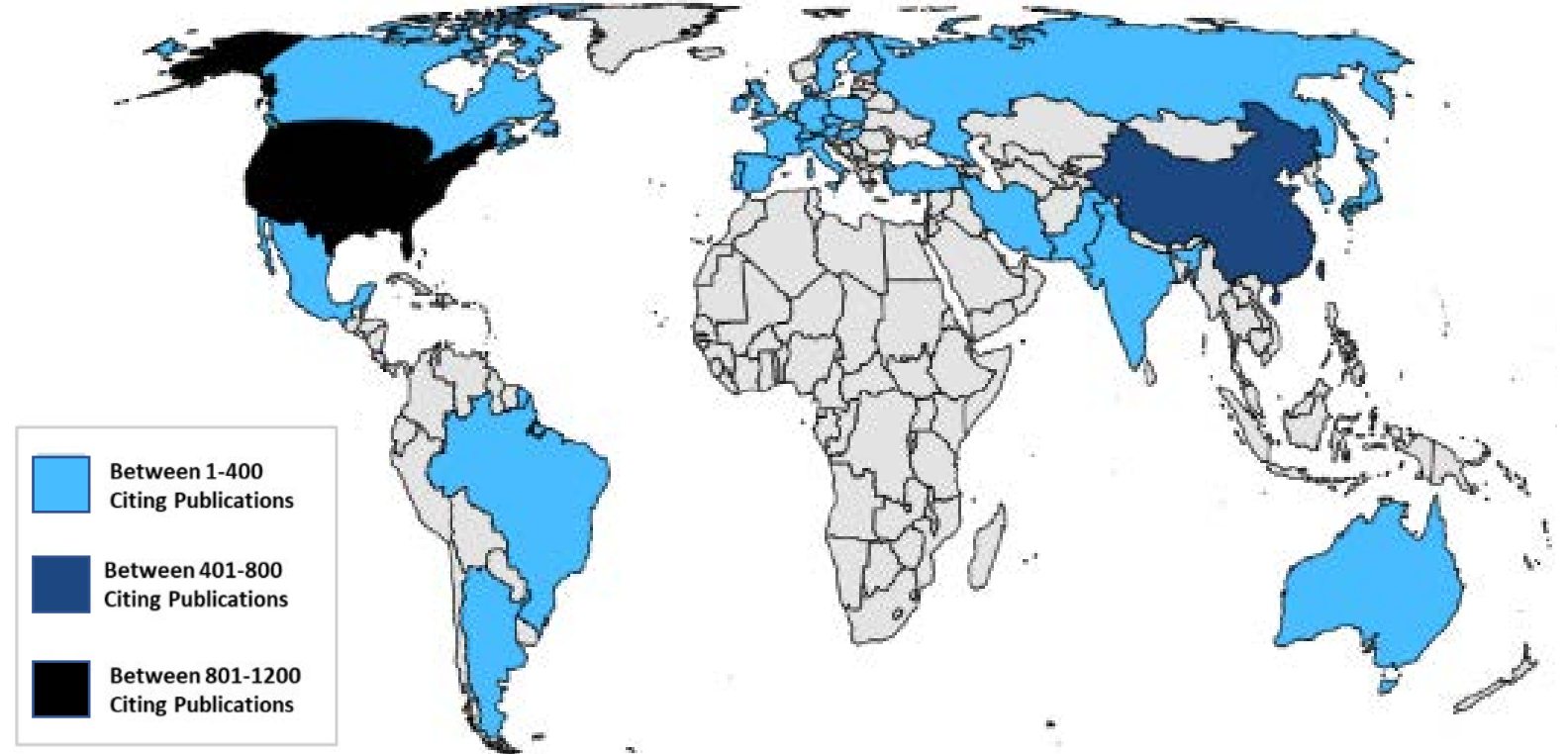
Citation of GSP Resources



Citation of GSP Resources

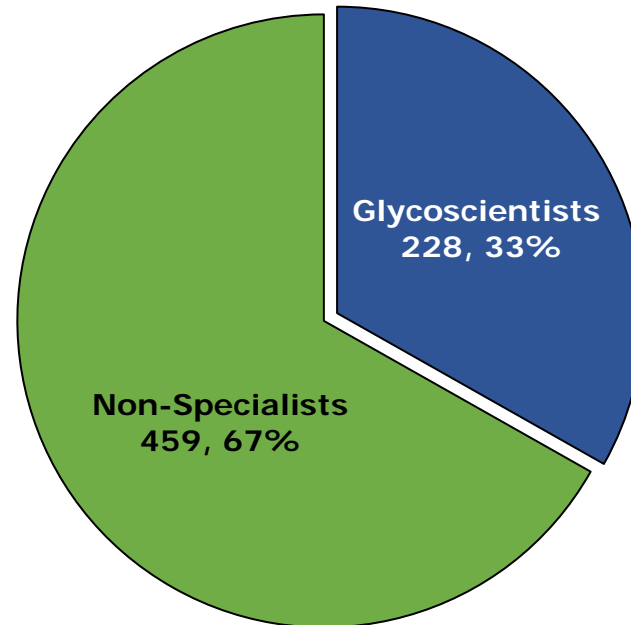
The countries with the most citing authors were:

- United States (33%)
- China (23%)
- Germany (6%)
- United Kingdom (5%)
- Japan (4%)



Citation of GSP Resources

Glycoscientists and Non-Specialists in Sample (n=687)



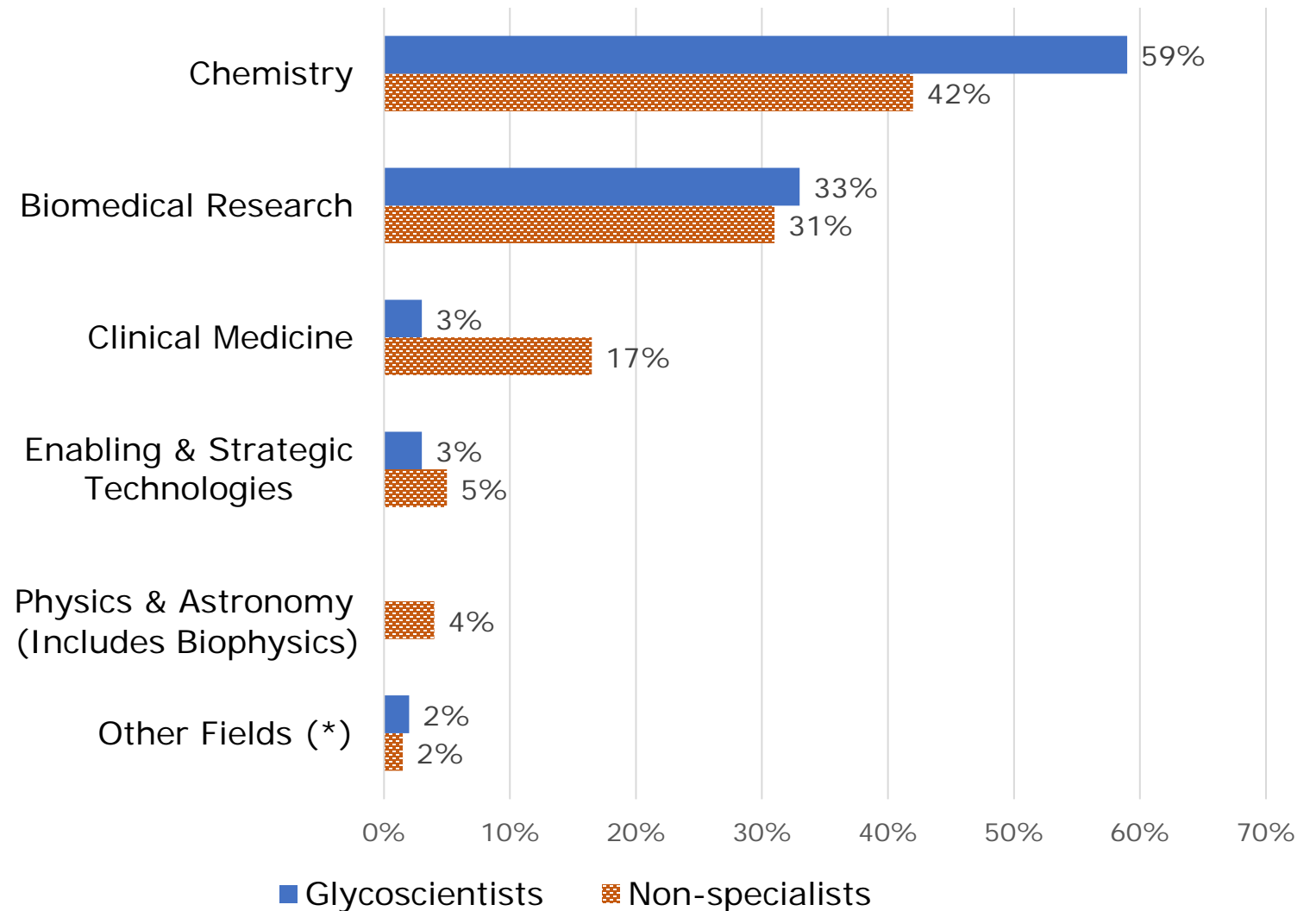
Citation of GSP Resources

GSP Initiatives Cited

GSP Initiative	Glycoscientist Citing Publications (n=620)	Non-Specialist Citing Publications (n=640)
Tools	318 (51%)	404 (63%)
Synthesis	328 (53%)	227 (35%)
Informatics	16 (2%)	21 (3%)

Citation of GSP Resources

Sampled Citing Publications Corresponding Author Classifications



Use of GSP Resources | Interviews

Biochemistry

- Organic Material Science
- Chemical Biology (n=6)

- *Use GlyGen to identify enzymes that create glycans of interest*
- *Cleave glycans from glycoproteins inexpensively and easily using protocol developed by GSP research*

Biology

- Protein Biology
- Microbiology (n=4)

- *Identify and bind chemokines using GAGs*
- *Use GSP-developed products to label amino acids to study cell division*

Immunology

- Immune Engineering
- Gastrointestinal Immunology (n=4)

- *Use GSP products to turn bacterial polysaccharides into nanoparticles*
- *Identify glycan modifications using GSP-developed probes*

Clinical Research

- Pulmonary care
- Nephrology (n=6)

- *Examine how glycosylation profiles lead to liver disease*
- *Conduct omic analyses of kidney biopsies*

Use of GSP Resources

Utility of GSP resources

GSP resource quality

Findings	NS	G
High degree of innovation and quality among GSP resources	14	4
GSP resources are scientifically rigorous	11	4

Both the method development as well as the analytical, the data analysis tools. [Innovation] is what [the GSP is] about. They're really high on that.
(Glycoscientist)

One thing that was done that was very nice is that [the probe developer] established collaborations with different scientists who work on different bacteria to show that it's not just E. coli, which is the best studied organism. You could use them for many different bacteria... I thought the development was rigorous and it worked very well. (Non-Specialist)

Non-specialist n=15, Glycoscientist n=5

Use of GSP Resources

Utility of GSP resources

Value added by GSP resources

Findings	NS	G
GSP resources made research possible	11	4
GSP resource shaped research focus	6	1
GSP resources improved glycoscience knowledge among non-specialists	7	0
GSP resources simplified and expedited research	3	4

Non-specialist n=15, Glycoscientist n=5

[The GSP resource is] invaluable, in a way, because there's no other way for us to look at interactions between these different molecules. There are experimental methods, which are very targeted, whereas this, using computational methods, enables you to screen large numbers of molecules. That's really the unique strength. (Non-specialist)

My interactions with the glycobiology community have largely shaped the way my laboratory has gone over the past 10 years. We had a lot of success looking at vascular biology but then we pivoted towards looking more at glycans. And it's fundamentally changed the scope of my lab. (Non-Specialist)

Use of GSP Resources

Utility of GSP resources

Challenges encountered

Findings	NS	G
Scientific limitations of GSP resources	6	2

[The challenge is] the need for still more refined tools. [My research] efforts... have not yet led to the answers that we seek. In this particular example, the [GSP] tools were developed to study mammalian or human-like carbohydrates, and what we study are bacterial carbohydrates... so the translation of the tools to bacterial carbohydrates has not been straightforward, a need still exists. (Glycoscientist)

I had my proteins of interest. We built them into [my collaborator's] assays and he had the expertise to make the molecular glycans that we were testing them against, but how to make that assay work with this new combination required trial and error... We found the best one... but it did take that time and effort to try two other methods that did not work as well. (Non-specialist)

Non-specialist n=15, Glycoscientist n=5

Q3. To what extent was the GSP successful in making glycoscience research resources available to the biomedical research community?

Facilitating access to glycoscience

Accessibility of GSP resources

Facilitating the adoption of GSP resources

Findings	NS	G
Connections and collaborations	6	2

[My collaborators'] willingness to share the materials, and undertake a collaboration, absolutely helped, or we wouldn't have been able to even start. (Glycoscientist)

I think the only thing I would like to tell you is truly the collaborative nature of the people that I work with and how none of this would've been possible. Taking the time to explain something to an immunologist. I think that's a strength. (Non-Specialist)

Non-specialist n=15, Glycoscientist n=5

Facilitating access to glycoscience

Accessibility of GSP resources

Hindering the adoption of GSP resources

Findings	NS	G
User limitations	6	2
Funding limitations	5	0

It's hard to make glycoscience tools for the non-expert... The technical details and the level of familiarity with glycoscience in general is a high bar to start with. Some of the tools when they first started... were really great, if you were already an expert in the field... Some of them are still very niche, and so they're not really applicable to a broad variety of platforms. (Glycoscientist)

It is time consuming to synthesize those probes and takes a lot of money and [my collaborators'] time. We are being very cautious about [using] them in the best way we can and that sometimes can limit how much we can do. (Non-Specialist)

Non-specialist n=15, Glycoscientist n=5

Facilitating access to glycoscience

Impact of GSP resources on field of glycoscience

GSP resource contribution to the field of glycoscience

Findings	NS	G
Provided valuable tools	N/A	4
GSP expanded glycoscience field	N/A	3

*[The GSP] creating a variety of different approaches and analysis types is really pushing the field forward and allowing us to measure things that we couldn't measure before.
(Glycoscientist)*

*Probably the biggest overall impact would be enabling more laboratories to engage in the study of glycans that if these tools and approaches weren't available, they would not be pursuing glycans as part of their research.
(Glycoscientist)*

Non-specialist n=15, Glycoscientist n=5

Facilitating access to glycoscience

Impact of GSP resources on field of glycoscience

Impact of GSP resource on researchers' future funding

Findings	NS	G
Foundation for future funding	13	3

[The resource has] allowed us to have the basic tools and understanding of the tools so that we can elevate the level of the science we're performing... And in fact, I am right now submitting another grant to NIH to use it further.
(Non-Specialist)

[The GSP resource] has enabled us to demonstrate expertise in a new tool that we didn't have expertise in before. It's enabled us to establish new and, hopefully, ongoing collaborations that will enable us to submit strong multidisciplinary grant applications. And, obviously, it's also provided us with key preliminary data that we can use to support the scientific premise of future proposals.
(Non-specialist)

Non-specialist n=15, Glycoscientist n=5

Analysis Limitations

- Interview findings are representations of stakeholders' perceptions, but they are not generalizable to all stakeholders involved in the GSP.
- Citations were examined as proxies for awareness and utilization of GSP-resource publications
- A subsample of 750 corresponding authors of citing publications were identified for further analysis and classification as glycoscientists or non-specialists. Inferences about the full sample of authors on all citing publications cannot directly be made based on the corresponding author sample.

Key Takeaways

- The GSP resources were described as scientifically rigorous, highly innovative, and high quality by most interview participants.
- GSP resources provided value to interview participants by advancing their research, shaping how they conduct their research, improving their Glycoscience knowledge, and making research easier and faster.
- Glycoscientists perceived that the GSP provided valuable tools to researchers and expanded the field of Glycoscience.
- The GSP-facilitated collaborations were valuable resources for interview participants.
- Factors like going through a learning curve in a new field, technological limitations, and the nicheness of tools hindered the adoption of GSP resources.

Thank you to:

- The researchers who participated in the evaluation
- Ripple Effect
- The NIAID PP&E Branch
- Douglas Sheeley and Rachel Britt, Office of Strategic Coordination



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