

Carbohydrate Ligands

Receptor-Mediated Drug Delivery & Custom Synthesis

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Carbohydrates In Therapeutic Development & Drug Delivery

Carbohydrates (glycans) are found on the majority of cell surface and circulatory proteins and are also conjugated to cell surface lipids where they are involved in a host of processes including cell recognition, cell adhesion, fertilization, and immune function. Little wonder that carbohydrates are being applied to therapeutic development & drug delivery.

Exploiting lectin/carbohydrate-mediated drug delivery through use of glycobiology may offer a means of addressing the specific challenge of delivering and targeting difficult therapeutic molecules. The idea of using lectin-carbohydrate interactions to mediate cell targeting and cellular uptake of molecules in general has been under intense investigation. There is potential for carbohydrate ligands to specifically introduce and activate therapeutic macromolecules into diseased cells in a manner that allows for specific and controlled modulation of protein production. Cell-specific delivery of therapeutic agents via carbohydrate ligand targeting has gained interest due to its potential for increased efficacy and reduced side effects.

Sussex Research Laboratories Inc. is the leading commercial source of synthetic, well-defined carbohydrate ligands such as PEGylated glycosides. These are multi-purpose, functionalized products that enable researchers to modify macromolecules, surfaces and nanoparticles with carbohydrates via simple polyethylene glycol (PEG) or alkyl linker/spacer systems. In contrast to alkyl, PEG linkers are amphiphilic which reduces linker hydrophobic interactions with macromolecules and surfaces.

Custom Synthesis: The number and variety of applications for carbohydrates in modern research and development is staggering. Sussex Research is highly active in the custom and contract synthesis of carbohydrate systems for specific research, drug and vaccine development projects. You pick the glycan, the linker system and the functional group, and we'll make it happen.

GLOBAL LEADER IN CARBOHYDRATE SYNTHESIS

Translating complex carbohydrate chemistries into unique, leading-edge products that enable researchers to explore and exploit glycobiology applications that promote human health.

PRODUCTS & SERVICES

Products

We take pride in conceptualizing, developing, and manufacturing a novel portfolio of carbohydrate products. From functionalized carbohydrate molecules to glycoconjugates and glucuronide metabolites, the Sussex product portfolio is both unique and wide-ranging.

Custom Synthesis

We are well known for our custom synthesis capabilities which utilize our core carbohydrate synthetic expertise. We provide synthesis solutions for pharmaceutical, biopharmaceutical, diagnostic and vaccine applications that require elements of glycotecnology.

Contract Research & Development

We participate as a trusted partner in a wide variety of pharmaceutical R&D projects ranging from early-stage drug delivery & development to polysaccharide and glycoconjugate vaccine development.

Structural Analysis

We draw on extensive knowledge in Nuclear Magnetic Resonance (NMR) Spectroscopy, Mass Spectrometry (MS), purification and subsequent chemical characterization of carbohydrate and isotope-labeled molecules.

Specializing in GalNAc for drug targeting, glycans for drug discovery, glycopeptides, and carbohydrate ligands for immunotherapeutic development.

Carbohydrate, glycoconjugate or glycan target? We are ready to take on your specific synthetic challenge!

COMPANY PROFILE

Sussex Research Laboratories Inc. has been a trusted provider of carbohydrate-based products and synthetic services since 1996. A spin-off of the National Research Council (NRC) of Canada, the company is housed at NRC's Industry Partnership Facility within NRC's flagship facility in Ottawa, Canada. This facility provides excellent infrastructure for organic synthetic chemistry including high field NMR & fermentation facilities.



NRC Facility at Ottawa, Ontario, Canada

In mammals, sugars are most commonly found as glycoconjugates, the most abundant being the glycoproteins, proteoglycans and glycolipids. These are predominantly located on cell membranes but also in secreted fluids where they modulate or mediate a host of events in cell-cell and cell-matrix interactions.

WHY GLYCOTECHNOLOGY?

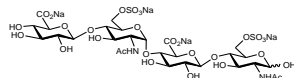
Glycoconjugation of a biotherapeutic (peptide, protein or antibody) may confer increased therapeutic efficacy via:

- > Superior stability
- > Increased bioavailability
- > Longer in-vivo half-lives
- > Higher aqueous solubility
- > Enhanced target resolution

Glycans (unconjugated oligosaccharides) can also mediate various physiological processes. The synthetic pentasaccharide, Fondaparinux, chemically related to Heparin, is also a potent antithrombotic drug.

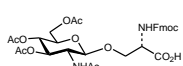
GENERAL AREAS OF FOCUS

1. **Oligosaccharide/Glycan Synthesis:** Highly pure synthetic glycans for drug discovery and research rigorously characterized by modern spectroscopic methods.

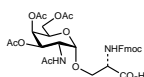


HEPARIN-LIKE TETRASACCHARIDE

2. **Glycoamino Acids:** The largest portfolio of O- and N-linked Fmoc glycoamino acids for glycopeptide synthesis or glycoconjugation of biologicals.

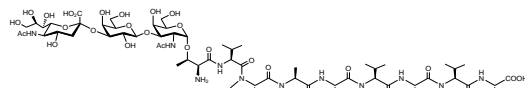


β -GlcNAc



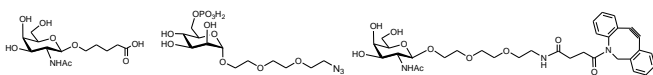
α -GalNAc (Tn-Antigen)

3. **Glycopeptides:** Portfolio of glycopeptides and custom synthesis – virtually any glycoform including biantennary structures). Numerous MUC1 glycopeptides.



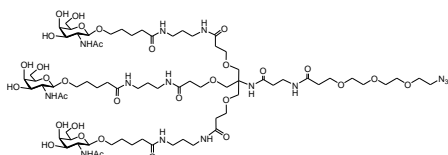
ANTIPROLIFERATIVE FACTOR (Frizzled-8 protein fragment)

4. **Carbohydrate Ligands – Targeting:** Portfolio of carbohydrates conjugated to functionalized linker systems for facile glycoconjugation of other molecules/particles.



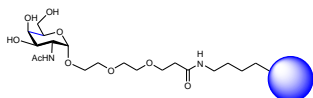
PEGYLATED OR ALKYL GLYCOSIDES (-N₃, -NH₂, -COOH, -SH, DBCO, -C≡CH...)

5. **GalNAc – ASGPR Targeting:** Portfolio of ligands for facile glycoconjugation to other molecules for targeting & delivery applications.



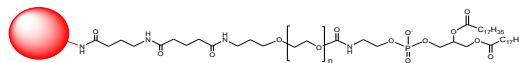
PEGYLATED OR ALKYL GalNAc – various functions available

6. **Neoglycoproteins / Glycoconjugates:** Portfolio of glycans, glycopeptides and other carbohydrate systems conjugated to BSA (or other carrier proteins upon request).



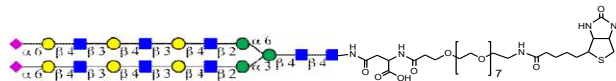
Multivalent α -GalNAc related to Tn antigen on BSA

7. **LNP Monomers:** Targeting ligands (glycans, peptides or small molecules) conjugated to PEGylated lipids allow for Lipid Nanoparticle (LNP) formulation and targeted drug delivery.



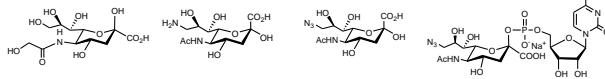
PEG(2000)-DSPE conjugated to a glycan or peptide payload

8. **Biotinylated Glycans:** Portfolio of biotinylated glycans designed for study of protein-carbohydrate interactions across various applications.



6'-Sialyl tri-LacNAc N-Glycan (Biantennary)

9. **Sialic Acid Derivatives:** N-modified sialic acids such as Neu5Gc. 9-hydroxy modifications (9-azido, 9-amino, 9-amido...).



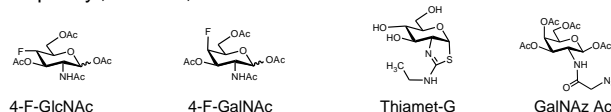
Neu5Gc

9-Amino

9-Azido

9-Azido sialic acid

10. **Modified Saccharides:** Portfolio/custom synthesis of glycosidase inhibitors (anhydro, fluorinated, 5-thio, thiazole and 2-thioisocyanate derivatives) as well as glycals, amines, azides, nitrophenyl, GalNAz, etc.



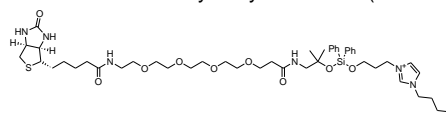
4-F-GlcNAc

4-F-GalNAc

Thiamet-G

GalNAz Ac₄

11. **Enrichment reagents:** Cleavable Biotin Probes for labeling of biomolecules via azide-alkyne cycloaddition (Click Chemistry).



Azide Analogue, Alkyne also available. Picolyl Azide also available.

Contract Research, Synthesis, Process Development

We welcome projects involving research, development, and optimization of synthesis methods, scale-up and manufacturing strategies for all kind of carbohydrate and small molecules. Applications include:

- > Vaccine Development
- > Drug Development
- > Drug Targeting/Delivery
- > Polysaccharide Chemistry
- > Drug Half-life Extension
- > Antibody Development
- > Protein/Antibody Modification (ADC)
- > GalNAc Ligand Development

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CARBOHYDRATE LIGANDS

Sussex Research has an extensive selection of functionalized carbohydrate ligands with various spacer/linker systems. These enable facile introduction of carbohydrate-based recognition elements onto a variety of molecules including small molecules, surfaces, nanoparticles, peptides, proteins, antibodies, liposomes, and oligonucleotides.

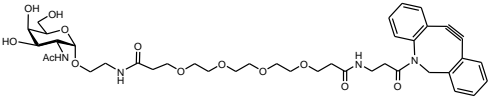
Carbohydrate Ligands with functionalized Ethylene Glycol (PEG) linker/spacers:

Please see our website for a more comprehensive listing.

Alkyne Function for Click Chemistry (Reactive with azides):

PE131000	α -GalNAc-PEG3-alkyne	 <p>α-GalNAc-PEG3-Alkyne</p>
PE131010	β -GalNAc-PEG3-alkyne	
PE231000	β -GlcNAc-PEG3-alkyne	
PE431000	β -Gal-PEG3-alkyne	
PE531000	β -Glc-PEG3-alkyne	
PE631000	α -Man-PEG3-alkyne	

Strained Alkyne Function for Copperless Click Chemistry (Reactive with azides):

PE131020	β -GalNAc-PEG3-DBCO	 <p>α-GalNAc-PEG4-DBCO DBCO = dibenzocyclooctyne</p>
PE141000	α -GalNAc-PEG4-DBCO	
PE941000	LacNAc-PEG4-DBCO	
PE041000	Neu5Aca(2,6)LacNAc-PEG4-DBCO	
PE041010	Biphenyl Neu5Aca(2,6)LacNAc-PEG4-DBCO	
MV100040	Triantennary GalNAc-PEG4-DBCO (Hepatocyte Targeting)	

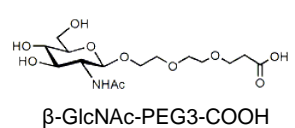
Amine Function (Reactive with carboxylic acids):

PE133000	α -GalNAc-PEG3-Amine	 <p>α-Man-PEG3-Amine</p>
PE133010	β -GalNAc-PEG3-Amine	
PE233000	β -GlcNAc-PEG3-Amine	
PE433000	β -Gal-PEG3-Amine	
PE533000	β -Glc-PEG3-Amine	
PE633000	α -Man-PEG3-Amine	

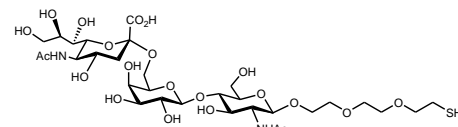
Azide Function for Click Chemistry (Reactive with alkynes):

PE134000	α -GalNAc-PEG3- N ₃	 <p>α-Man-6-phosphate-PEG3-N₃</p>
PE134010	β -GalNAc-PEG3- N ₃	
PE234000	β -GlcNAc-PEG3- N ₃	
PE434000	β -Gal-PEG3- N ₃	
PE534000	β -Glc-PEG3- N ₃	
PE634000	α -Man-PEG3- N ₃	
PE634010	α -Man-6-phosphate-PEG3-N ₃	
PE934000	β -Lac-PEG3- N ₃	
PE934010	LacNAc-PEG3-N ₃	

Carboxylic Acid Function (Reactive with amines):

PE132000	α -GalNAc-PEG3-COOH	 <p>β-GlcNAc-PEG3-COOH</p>
PE132010	β -GalNAc-PEG3-COOH	
PE232000	β -GlcNAc-PEG3-COOH	
PE432000	β -Gal-PEG3-COOH	
PE532000	β -Glc-PEG3-COOH	
PE632000	α -Man-PEG3-COOH	
PE942000	β -Lac-PEG4-COOH	

Thiol (Sulfhydryl) Function (Reactive with maleimides):

PE135000	α -GalNAc-PEG3-SH	 <p>NeuAc(2,6)LacNAc-PEG3-SH</p>
PE135010	β -GalNAc-PEG3-SH	
PE235000	β -GlcNAc-PEG3-SH	
PE435000	β -Gal-PEG3-SH	
PE535000	β -Glc-PEG3-SH	
PE635000	α -Man-PEG3-SH	
PE935000	β -Lac-PEG3-SH	
PE935010	LacNAc-PEG3-SH	
PE035010	NeuAc(2,3)LacNAc-PEG3-SH	
PE035020	NeuAc(2,6)LacNAc-PEG3-SH	

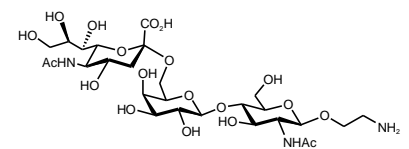
Maleimide (MAL) Functionalized (Reactive with thiols and maleimides):

PE136000	α -GalNAc-PEG3-MAL
PE136010	β -GalNAc-PEG3-MAL
PE806000	α -L-Rha-PEG12-MAL

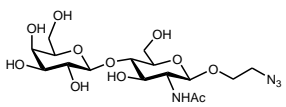
Carbohydrate Ligands with alkyl spacers:

Carbohydrate ligands on short, functionalized alkyl linker/spacers.

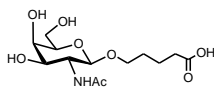
Amine Functionalized (Reactive with carboxylic acids):

AG123000	2-Aminoethyl 2-acetamido-2-deoxy- α -D-galactopyranoside	 <p>2-Aminoethyl (Neu5Ac α2-6Gal β1-4GlcNAc) A targeting ligand for CD22 Lectin</p>
AG223000	2-Aminoethyl 2-acetamido-2-deoxy- β -D-glucopyranoside	
AG423000	2-Aminoethyl β -Galactopyranoside	
AG423005	2-Aminoethyl α -Galactopyranoside	
AG523000	2-Aminoethyl β -Glucopyranoside	
AG623000	2-Aminoethyl α -Mannopyranoside	
AG823000	2-Aminoethyl α -Rhamnoside	
AG923000	2-Aminoethyl β -Lactopyranoside	
AG923010	2-Aminoethyl β -LacNAc	
AG023000	2-Aminoethyl (Neu5Ac α 2-6Gal β 1-4GlcNAc)	

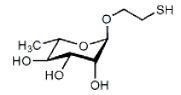
Azide Functionalized for Click Chemistry (Reactive with alkynes):

AG124000	2-Azidoethyl 2-acetamido-2-deoxy- α -D-galactopyranoside	 <p>2-Azidoethyl β-LacNAc</p>
AG124010	2-Azidoethyl 2-acetamido-2-deoxy- β -D-galactopyranoside	
AG224000	2-Azidoethyl 2-acetamido-2-deoxy- β -D-glucopyranoside	
AG424000	2-Azidoethyl β -Galactopyranoside	
AG424005	2-Azidoethyl α -Galactopyranoside	
AG524000	2-Azidoethyl β -Glucopyranoside	
AG624000	2-Azidoethyl α -Mannopyranoside	
AG824000	2-Azidoethyl α -Rhamnoside	
AG924000	2-Azidoethyl β -Lactopyranoside	
AG924010	2-Azidoethyl β -LacNAc	
	Lewis X- β -propylazide	

Carboxylic Acid Functionalized (Reactive with amines):

AG152000	4-Carboxybutyl 2-acetamido-2-deoxy- α -D-galactopyranoside	 <p>4-Carboxybutyl 2-acetamido-2-deoxy-β-D-galactopyranoside A targeting ligand for Asialoglycoprotein Receptor</p>
AG152010	4-Carboxybutyl 2-acetamido-2-deoxy- β -D-galactopyranoside	
AG252000	4-Carboxybutyl 2-acetamido-2-deoxy- β -D-glucopyranoside	
AG452000	4-Carboxybutyl β -Galactopyranoside	
AG452005	4-Carboxybutyl α -Galactopyranoside	
AG552000	4-Carboxybutyl β -Glucopyranoside	
AG652000	4-Carboxybutyl α -Mannopyranoside	
AG642010	4-Carboxybutyl 6-O-phosphate- α -D-mannopyranoside	
AG852000	4-Carboxybutyl α -Rhamnoside	
AG952000	4-Carboxybutyl β -Lactopyranoside	

Thiol (Sulfhydryl) Functionalized (Reactive with thiols and maleimides):

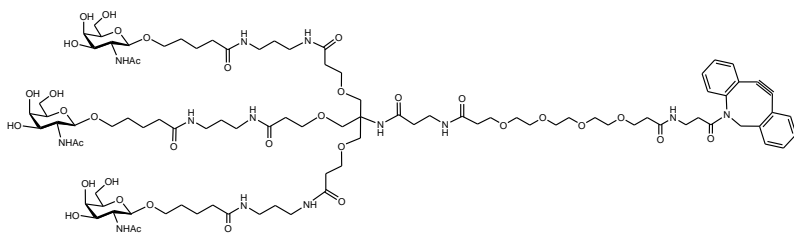
AG155000	α -TF-PEG6-C6-SOC(O)CH ₃ -TF Antigen with Pentanethiol linker (PEG6 as a spacer)	 <p>2-Thioethyl α-Rhamnopyranoside</p>
AG155005	β -TF-PEG6-C6-SOC(O)CH ₃ -TF Antigen with Pentanethiol linker (PEG6 as a spacer)	
AG225000	2-Thioethyl β -N-Acetylglucosamine	
AG425000	2-Thioethyl β -Galactopyranoside	
AG425005	2-Thioethyl α -Galactopyranoside	
AG525000	2-Thioethyl β -Glucopyranoside	
AG525005	2-Acetylthioethyl β -Glucopyranoside	
AG625000	2-Thioethyl α -Mannopyranoside	
AG825000	2-Thioethyl α -Rhamnopyranoside	
AG925000	2-Thioethyl β -Lactopyranoside	

Trivalent Carbohydrate Ligands with linker/spacers:

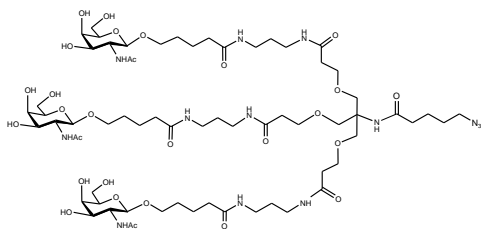
Targeting ligands enable efficient hepatic uptake of conjugate molecules via the Asialoglycoprotein Receptor (ASGPR). This has been particularly noteworthy as an emerging approach to delivery of siRNA-based therapeutics.

Triantennary saccharides (any functionality such as PEG or Alkyl linker/spacer):

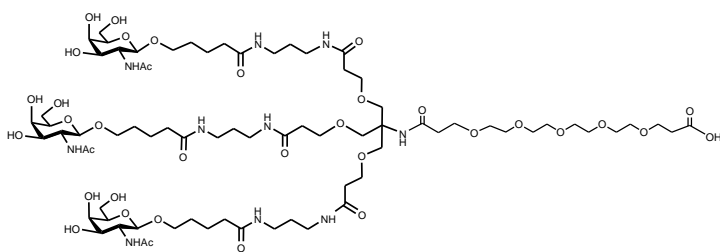
Azide reactive For Copperless Click Chemistry:



Alkyne-reactive for Click Chemistry:



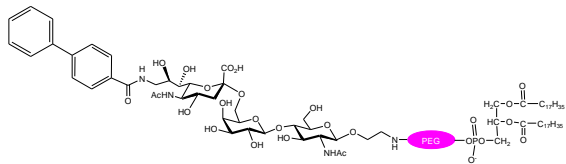
Amine-reactive:



Many more tri-glycosylated ligands available – please inquire.

Carbohydrate Ligand Liposome Systems:

Siglec Ligand - Exploiting the sialic acid binding immunoglobulin-type lectins for drug targeting.

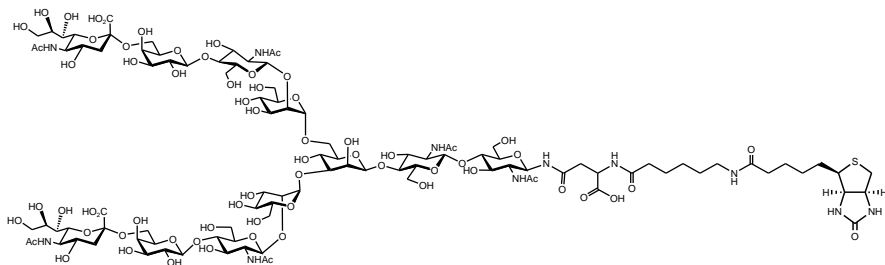


Example: CD22 Ligand-conjugated PEGylated Lipid (Liposome monomer) for delivery

Complex Carbohydrate Ligands:

Complex Carbohydrates based on high Mannose and biantennary glycans. Sussex Research will prepare the functionalized glycan of your choice.

Example of a Biantennary System (A2 Glycan):



Custom Synthesis

Sussex Research Laboratories Inc. welcomes projects which utilize core expertise in carbohydrate synthesis. We specialize in multi-step custom synthesis of carbohydrate and glycoconjugate systems.

Inquiries: info@sussex-research.com

Orders: orders@sussex-research.com

www.sussex-research.com

