# Carbohydrate Mimetics in Precision Medicine

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**CO-OWNERS:** Florida International University

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**N° PRIORITY:** US 17/136,839

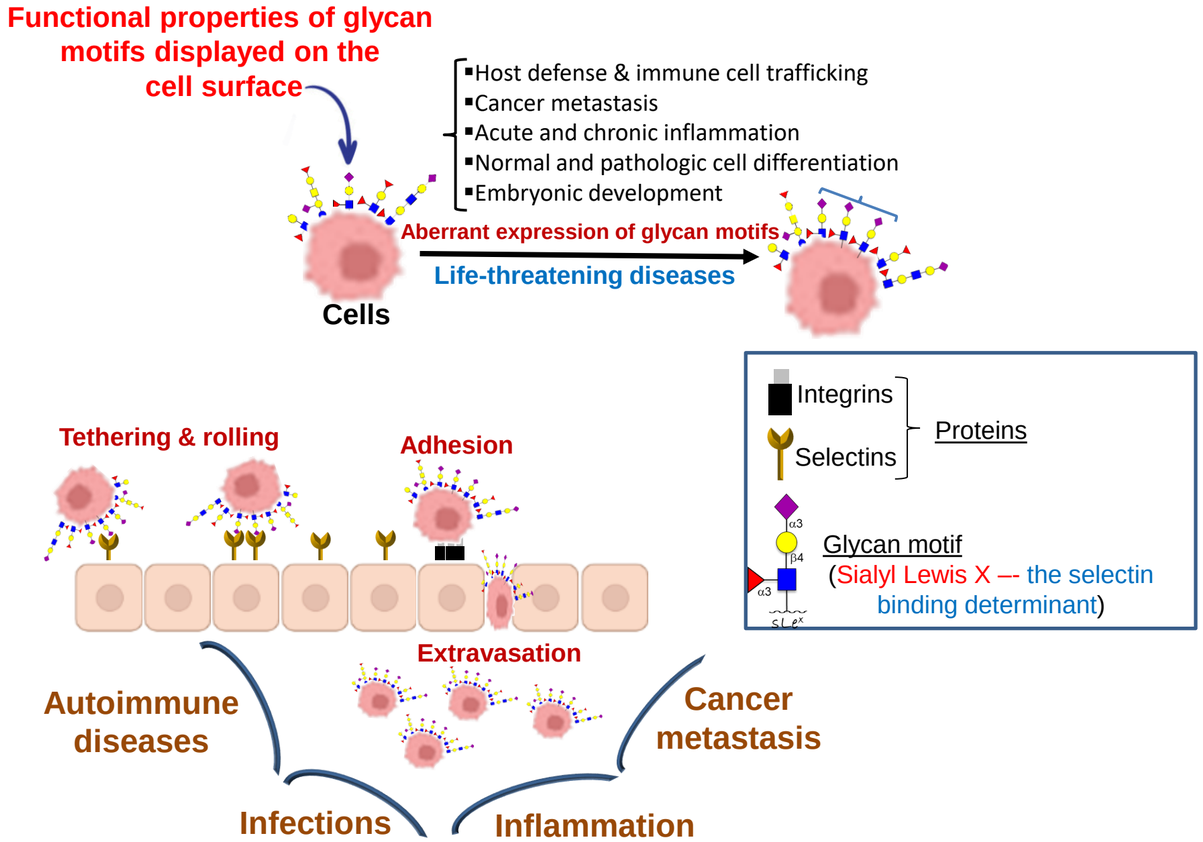
**GRANTED ON: -**

**PATENT FAMILY: WO2022146978A1**

# The Technology

The patent application protects nontoxic small molecules (glycomimetics), easily obtained from natural compounds (carbohydrates), which can be used for **personalized treatment of glycan-related diseases**. These mimetics possess exquisite specificity for certain enzymes, known as fucosyltransferases, FTs, whose dysregulation is at the heart of many burdensome diseases. The highly specific inhibition of aberrant expression of certain FTs and their downstream products (glycans), while allowing untargeted FTs to continue to play their physiological roles unhindered, holds great promise for a new generation of precision medicine. The field of glycosciences has witnessed many recent discoveries and advances that have revealed the key roles of glycans in the organization, function, and pathology of eukaryotic cells, as well as providing biomarkers of burdensome diseases. Therefore, in the era of precision therapy, **glycan-directed therapies** have the potential to be considered as the **next generation of drugs** that can provide innovative targeted therapeutic options. In this context, the present invention aims to develop glycan-directed therapies through personalized modification of cellular glycosylation without manipulating the genetic machinery of the cell. Glycoengineering at this level requires the development of nontoxic inhibitors with elegant specificity for a given enzyme (glycosyltransferase) that regulates the expression of specific glycans on the cell surface, ensuring the absence of effects on off-target enzymes. Fucosyltransferases (FTs), particularly -1,3-FTs, are key enzymes involved in the biosynthesis of glycans on the cell surface that confer critical cellular functions in a wide variety of biological contexts (leukocyte trafficking, metastasis, host defense, human fertilization, cell adhesion, immune and neural cell differentiation). Indeed, regulated-1,3-FT(s) activity, resulting in aberrant overexpression of key glycans, is etiologic in several human diseases. Viewed from this perspective alone, -1,3-FTs are rational targets for drug design, and downregulation, or disruption, of their activity may provide **therapeutic relief for a multitude of life-threatening diseases**. The glycomimetics of this invention provide the first known selective inhibition of FTs. They inhibit only the targeted FTs and have no effect on other (nontarget) glycosyltransferases, resulting in the generation of only the desired glycan products. Notably, these mimetics are easily produced by a modular methodology that allows structural diversification and thus the assembly of a **library of compounds** aimed at improving efficacy.

# Images

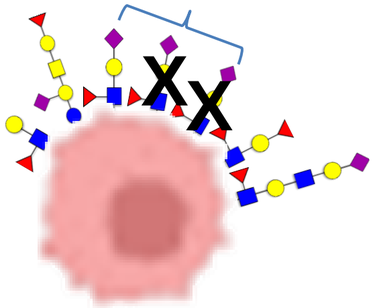

Functional properties of glycan motifs displayed on the cell surface
Host defense & immune cell trafficking
Cancer metastasis
Acute and chronic inflammation
Normal and pathologic cell differentiation
Embryonic development
Cells
Aberrant expression of glycan motifs
Life-threatening diseases
Integrins
Selectins
Proteins
Glycan motif
(Sialyl Lewis X –- the selectin binding determinant)
Tethering & rolling
Adhesion
Extravasation
Autoimmune diseases
Cancer metastasis
Infections
Inflammation

# Images

**Custom modification of cellular glycosylation without genetic manipulation of target cells**

***AIM*: Creation of a library of NON-TOXIC small molecule inhibitors of key cell enzymes ("glycosyltransferases") whose overactivity results in the aberrant expression of specific glycans that engender disease processes**

Inhibition of the aberrant expression of disease-causing glycans




**Selectivity** → NO off-target effect(s)

**Manufacturing process** → Easy access to a library of compounds

# Images

## INNOVATION OF THE DISCOVERY

Targeting aberrant glycosylation: A New Road for Drug Development

**PERSONALIZED** treatment of a multitude of life-threatening diseases
(Cancer, Inflammation and Autoimmune Diseases)

Therapeutic options that can act synergistically with current approaches

GlycFluoNano Lab

## WHY “GLYCOMIMETICS”?

These are small molecules that mimic the structure of native carbohydrates

**Therapeutic efficacy:** Enhanced selectivity & potency; improved pharmacokinetic properties

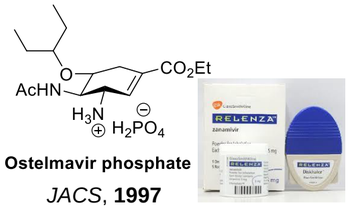
# Images

# Currently Marketed Glycomimetic Drugs

## Influenza A
**(Neuraminidase inhibitors)**


**Zanamivir**

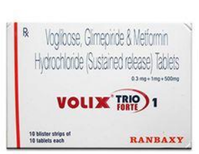
*Nature*, **1993**




**Ostelmavir phosphate**

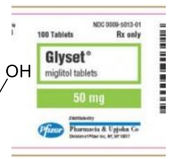
*JACS*, **1997**

## Diabetes
**(α-glycosidase inhibitors)**




**Voglibose**

*Curr. Med. Chem.*, **2006**




**Miglitol**

*Ann. Pharmacother.*, **2000**

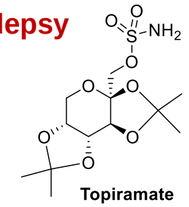
## Gaucher's disease


**Miglustat**

*Am. J. Hematol.*, **2005**

zavesca 100 mg

## Epilepsy




**Topiramate**

*J. Med. Chem.*, **1987**

## Thrombosis

**(Binding to antithrombin III)**

**Fondaparinux**
**Deltaparin**
**Ardeparin**
**Nardoparin**
**Enoxaparin**

*Semin. Thromb. Hemost.* **2003**

*N. Engl. J. Med.*, **1997**

# Industrial application

The potential applications of the technology are many; among the most relevant are all of the following:

1. Treatment of **inflammatory** processes
2. Treatment of **cancer**
3. Assistance in **fertilization processes**
4. Treatment of **autoimmune diseases**
5. Treatment of **degenerative diseases**

At the same time, the technology ensures the following advantages:

1. Ability to custom modify cellular glycosylation without genetic manipulation
2. Selective effect of the biological target
3. Easy access to a library of compounds
4. Glycomimetics are metabolically stable compared to natural carbohydrates
5. Innovative therapeutic options that can act synergistically with current approaches

# Future developments

The technology maturity of the patent can be schematized as follows:

1. Glycomimetics provide a significant effect in biological assays related to inhibition of expression of key glycans associated with cancer metastasis and inflammation (TLR3)
2. Glycomimetics are accessible by exploiting a modular synthetic strategy that allows structure diversification (compound library) (TRL4).

Research activities are currently underway to:

1. Evaluate the effect in different cancer cell models
2. Evaluate the effect of a dozen different glycomimetic derivatives, with the goal of improving their efficacy

The inventors are considering both licensing the patent application and creating a spin-off focused on the development of compounds based on glycomimetics, taking advantage of the possible benefit of knowing under exclusivity the methods and compositions of glycomimetic compounds with selective effect.

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