GlyTech, Inc.

Glycoscience for Better Health

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Our transformative and versatile glycan technologies have been developed with the aim of "harmonizing with nature."

Through these technologies, we endeavor to aid in the creation and practical application of compounds that will contribute extensively to the improvement of human health.

- Exploring the potential of glycans while creating new value
- Striving to develop innovative technologies to realize new value
- Helping to build a healthier world by creating new biotherapeutics and improving existing biotherapeutics

Elegant creation, in harmony with nature

To become fully functional biomolecules, proteins must undergo various chemical modifications inside the cell once they have been precisely translated from their associated genes. Since such modifications involve complicated processes, proteins with the same amino acid sequence can vary in their overall molecular structure. It is still extremely difficult to artificially control these vital post-translational modifications.

At GlyTech, we have succeeded in precisely controlling the post-translational modification known as glycosylation, the attachment of oligosaccharides (glycans) to proteins. To do this, we first efficiently extract basic glycan skeletons from natural materials before using chemical and enzymatic methods to convert them into a wide variety of other structures. The resulting inexpensive, high-purity glycan compounds can then be attached to proteins using our proprietary organic synthesis methods, allowing full control of the molecular structure of the final "glycoprotein."

We are dedicated to the continual ad of the highest elegance and quality.



We are dedicated to the continual advancement of these technologies to create products

Hiroaki Asai CEO, GlyTech, Inc.



We're helping to drive *glycosylated therapeutics* towards a future where they are on par with conventional biotherapeutics. Based on our own extensive experience of developing chemically glycosylated pharmaceuticals (glycosylated peptides, proteins, small molecules, etc.) and supported by our large-scale glycan production platform*, we offer a wide range of services suitable for every stage of the drug development process. *N-glycan production

Glycans with uniform structure and reliable quality

- Homogenous structures
- purity and quality • Suitable for direct use in drug development and
- biologics analysis

Purpose-oriented structural design

- Access to desired structures and specifications (Track records in *N*-glycans, O-glycans, free glycans, glycolipids, etc.)
- Tailoring of structures to meet specific objectives
- Custom synthesis of glycosylated peptides, proteins, and small molecules

- Versatile production

Drug development services supported by glycan manufacturing

Solutions to fit any R&D stage

Research stage

Proprietary platform-based services for seed compound search and glycan library-enabled optimization of seed and target compounds. Compounds modified with glycans can be expected to be highly unique drug candidates.

Discovery support

- Proprietary screening platform for seed compound discovery
- Glycosylation-based optimization of physicochemical properties and functionality
- Lead compound synthesis
- Structural characterization and analytical support

Pre-clinical support

- Synthetic process development for drug candidates (non-GMP)
- Production of drug candidates
- Analytical method development for drug candidates (non-GMP)

Development stage

Drug development services that make the most of our expertise in the production of glycopeptide drugs.

Clinical trial support

- GMP process development towards commercial manufacturing
- Production of drug substance for clinical trials
- Documentation support (Manufacturing, QA/QC and CMC documentation for regulatory filing, etc.)
- Quality control analytical method development

• Analytically confirmed structures with guaranteed

From basic research to clinical trial use

• 10 kg/year* glycan manufacturing system *N-glycan production from chicken egg • Glycoconjugate manufacturing (glycopeptides, glycoproteins, etc.)

Commercialization



Flexible customization



Glycans attached to the membrane proteins scattered across the surface of our cells are involved in various biological phenomena, such as cell signaling, identification (e.g., blood types), metabolism and protection, and virus infection. Meanwhile, glycans attached to secretory proteins, which most biopharmaceuticals are developed from, affect their blood stability, structure and function.

Membrane proteins

Developing new and improved therapies using naturally-occurring glycan structures





Glycans cover the surface of the cell in a hair-like coating (glycocalyx)



Glycans are being applied to cancer treatment R&D

The structures of glycans on the surface of cancerous cells undergo characteristic changes compared with those on non-cancerous cells. These are exploitable in cancer therapy, for example, as part of a cancer vaccine containing a cancer-specific glycan or a glycan-decorated section (glycopeptide) of a cancer protein as the antigen. Glycoproteins specifically produced by tumor cells are also used as diagnostic markers.



Biobetters have been made a reality

Erythropoietin (EPO), a therapeutic protein drug for renal anemia, is one biotherapeutic that has been developed into a "biobetter" using glycans. The original form of EPO contains four attached glycans. Using genetic modification, two extra glycans were added to improve the stability of EPO in the blood. This 6-glycan biobetter form can be used to reduce the burden on the patient by reducing the frequency of administration, and was marketed as a high-performance alternative.



Glycosylation has the potential to improve peptide formulations

Glycosylation has recently been reported to dramatically improve the physicochemical properties of insulin, a peptide hormone and the oldest biopharmaceutical, and could lead to better, more convenient formulations for patients.

Research is already underway on the application of targeted glycosylation to as-yet untapped seed compounds, such as peptide hormones, present in the human body.





We're developing glycosylated peptide drugs

Conventionally, modifications based on non-natural materials have been used to improve the properties of peptides with low in vivo stability to make them suitable as pharmaceuticals. However, such modifications may increase the risk of side effects, and lower risk methods are continually being sought. By using human-type glycans instead, we aim to develop highly safe drugs made up of components that are extremely close to biological structures.

Glycoengineering technologies for pharmaceutical applications

From familiar raw materials such as chicken eggs, we produce glycans at the quantities, quality and cost efficiency needed for pharmaceutical development and manufacturing. Using these highly pure glycans as starting materials, we have established an extensive library of glycan structures with a wealth of applications, not only in drug development, but also in the quality control and improvement of existing biopharmaceuticals.

GlyTech, Inc.'s Core Technologies



Functionalization of glycan reducing end



We're able to modify any of our glycans in our library to functionalize them for different uses. For example, by attaching labels used for analytical standards, our glycans can be used to detect more detailed differences in biopharmaceutical glycan structure with higher accuracy. In addition, by "activating" the glycan (like adding a molecular "glue"), it becomes possible to attach them to peptides / proteins to alter their properties.

Synthesis of glycopeptides/ glycoproteins

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We chemically synthesize glycan-modified peptides (glycopeptides) and proteins (glycoproteins) using our proprietary glycan library. Pharmaceuticals modified with glycans can be expected to have improved physicochemical properties (such as solubility and stability) while retaining the functionality of the original peptide or protein. We're already developing such glycosylated pharmaceuticals in our own pipeline and in partnership with other companies and institutions.

Glycosylation of various materials



Our glycosylation platforms aren't constrained by material type. Suitably activated glycans can be used to modify a variety of materials other than peptides and proteins. A diverse range of applications has been studied – not only the improvement of the physicochemical properties of glycosylated compounds, but also their transport to targeted tissues, and the creation of antigens for antibody discovery and development.

Development of new glycan production methods



We're continuously developing new ways of producing glycans from a wider range of raw materials and improving access to high-value and complex glycan structures. Keeping environmental issues in mind, we aim to incorporate green chemistry methods and make effective use of food by-products and industrial waste in our technologies.

GlyTech, Inc.

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Kyoto Head Office

| Established | April 2nd, 2012 |
|-----------------|-----------------|
| President & CEO | Hiroaki Asai |
| | |

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Company History

- 2002 Research collaboration initiated between Otsuka Chemical Co., Ltd. and Professor Yasuhiro Kajihara of Yokohama City University (currently Osaka University)
- Development of human N-linked glycan mass production methods begun with the support of the Japan Science and Technology Agency (JST) 2006
- Glycoengineering research laboratory established at Otsuka Chemical Co., Ltd. 2009
- 2011 Started joint research with Bachem Holding AG, Switzerland, to develop glycoprotein manufacturing technology
- 2012 With Prof. Yasuhiro Kajihara, published the first chemical synthesis of human interferon β in the Journal of the American Chemistry Society GlyTech, Inc. established as a subsidiary of Otsuka Chemical Co., Ltd.
- 2013 GlyTech, Inc. becomes independent from Otsuka Chemical Co., Ltd.
- Capital investment totaling approximately 600 million JPY raised 2014
- 2015 Glycosylated somatostatin analog (G-SRIF) co-development agreement signed with Nippon Shokubai Co., Ltd. Capital increase totaling approximately 800 million JPY raised by third-party allotment
- 2017 GlycoTargeting Research Laboratory established with Senior RIKEN Researcher Katsunori Tanaka through the RIKEN Baton Zone Program Early exploratory clinical trial of glycosylated somatostatin analog GT-02037 in healthy adults
- Capital increase totaling approximately 1 billion JPY raised by third-party allotment 2018
- Agreement signed with Yung Shin Pharmaceutical Industrial Co., Taiwan for the joint clinical development of G-SRIF 2019
- 2020 Phase 1 clinical trial of GT-02037 injection carried out in Japan Capital increase totaling approximately 500 million JPY raised by third-party allotment



Reagent sales and contract synthesis

- *N*-linked glycans and glycopeptides
- O-linked glycans and glycopeptides

Collaborations and partnerships

- Collaborative drug delivery research
- Glycopeptide design for enzyme activity evaluation
- Glycosyltransferase discovery, production and activity evaluation
- Conjugation of glycans to oligonucleotides
- Glycopeptide synthesis partnerships

Fee-for-service

- Improvement of peptide solubility via glycosylation
- Antibody sequencing analysis and glycan analysis
- Cyclic glycopeptide synthesis
- Conjugation of glycans to small molecules

API manufacturing

• *N*-linked glycans and glycopeptides

Example Projects and Achievements

• Glycopeptide library creation (single peptide sequence with varied glycan structure)



Glycan products

- Glycan standards for analysis
- Glycan reagents for R&D

Custom synthesis & API manufacturing

- Glycans
- Peptides/glycopeptides
- Proteins/glycoproteins
- Target compound glycosylation service

Analysis services

- Glycoprofiling (Identification of glycan structure, position)
- Peptide mapping
- Analytical method development and support

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