GlyTech, Inc.
Glycoscience for Better Health

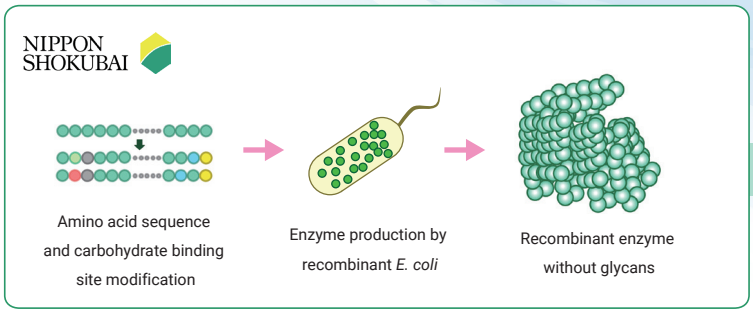
In partnership with NIPPON SHOKUBAI

Glycoprotein engineering

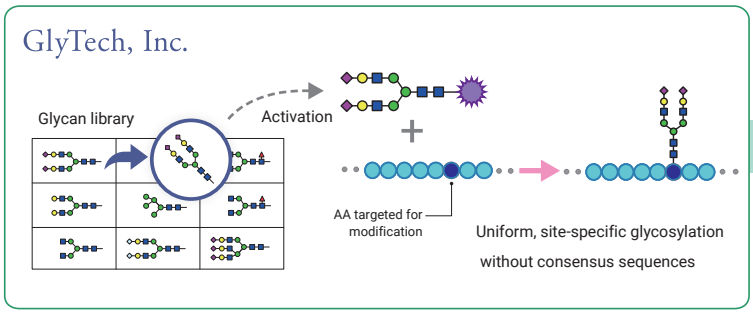
Bio-better enzyme development

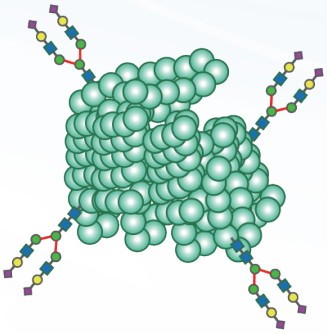
Many of the rare lysosomal storage diseases require treatment with enzyme replacement therapy (ERT). Many ERT drugs are transported to the appropriate organelle via attached mannose-6-phosphate or mannose-containing glycans. By combining E. coli expression and chemical glycosylation, we can create ERT-suitable enzymes previously only obtainable by animal cell expression.
We have used this approach to develop a new drug candidate for Gaucher disease and are now making this technology available for new drug discovery research.

Nippon Shokubai's enzyme production platform



GlyTech, Inc.'s chemical glycosylation platform





Glycoprotein with fully controlled glycan structure

Endocytosis-enabling technology via glycosylation with mannose-based glycans (Other glycan structures also available)

Our capabilities

GlyTech, Inc.

- Flexible model (reagent sales, contract research, drug substance production)
- Highly controllable glycan profiles
- Seamless scale-up from discovery/R&D to commercial manufacturing
- More than 50 N-glycan structures available

Nippon Shokubai Co. Ltd.

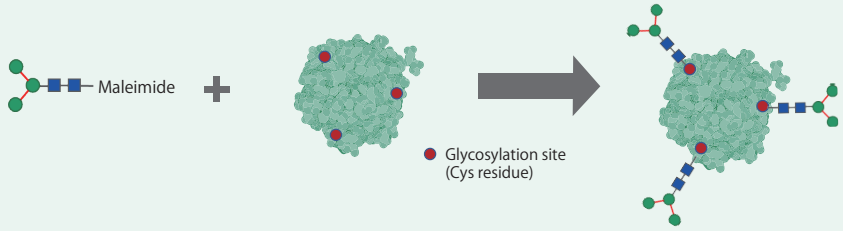
- Amino acid sequence optimization (for glycosylation, property improvement)
- Gene sequence optimization (for codon optimization)
- High density *E. coli* cultivation and overproduction technology

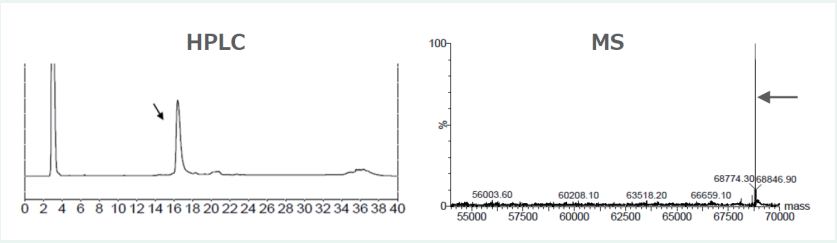
Creating drug development candidates for Gaucher disease
(Currently seeking joint development partners)

Development of human glycan-modified glucocerebrosidase

Nippon Shokubai's outstanding protein expression platform technology enhances stability and enzymatic activity, and prepares mutant proteins with anchoring sites for targeted glycosylation. Meanwhile, GlyTech's technology allows site-specific glycosylation to be carried out under mild conditions, to introduce desired glycans while maintaining the target's enzymatic activity.
By combining the strengths of both companies, we have succeeded in creating promising new drug development candidates.

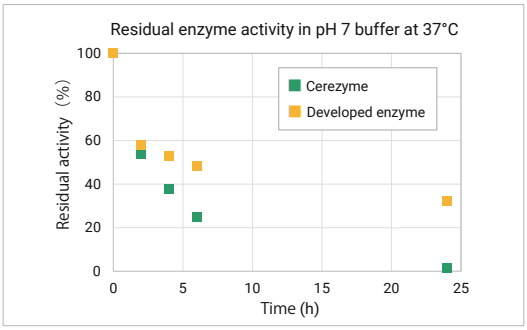
Chemical glycosylation of Cys-modified glucocerebrosidase

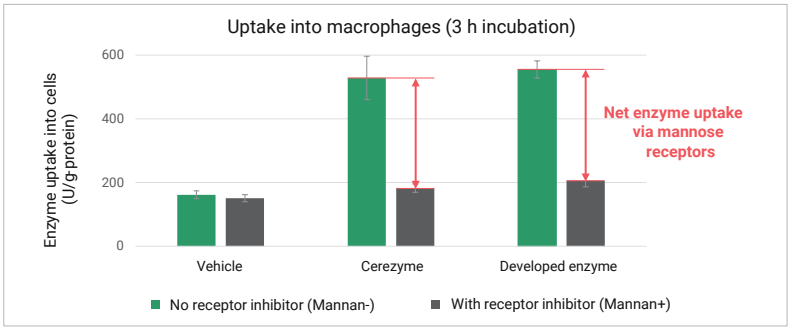




- **Avoids the challenges of animal cell expression (high-cost production processes, unstable supply issues, etc.)**
- **Ensures product quality by avoiding heterogeneity of glycans essential for enzyme transport**
- **Simplifies production, purification and quality control, reducing costs**

In vitro results





By combining E. coli-based protein expression and chemical glycosylation, we have been able to develop a highly pure glucocerebrosidase decorated with only mannose glycans. This new development candidate is more stable (L) under neutral conditions than the original drug (Cerezyme), and exhibits the same level of cellular uptake in vitro (R).

Why chemical glycosylation?

Bio-compatiblity

- Glycan structures that naturally occur in the human body
- Low risk of immunogenicity and unexpected toxicity

Site-specificity

- Sequence-independent design: freely select glycosylation site, structure, and number
- Highly pure and homogenous products simplify purification, QC, and characterization from R&D to manufacturing

Seeking a modification technology for your project? GlyTech, Inc. also provides enzymatic glycosylation services – contact us to speak with our experts!

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