

LICENSING OPPORTUNITY

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Efficient and cost-effective glycoengineering of glycoconjugates in bacteria

Patent Status

- Patent pending

Keywords

Glycoconjugates, therapeutic glycoproteins, N-linked glycosylation, oligosaccharyltransferase, glycoengineering, inhibitor design, *Campylobacter jejuni*, Guillain-Barré-Syndrom

Summary

X-ray structure of the oligosaccharyltransferase (OST) from *Campylobacter lari*, the central enzyme in the process of asparagine linked protein glycosylation, has been determined. The atomic 3D-model can be used for glyco- and protein engineering, i.e. to rationally design and modify the substrate specificities of the enzyme to produce therapeutically relevant eukaryotic glycoconjugates in prokaryotes of high homogeneity. In addition, the structure can be used to design and identify inhibitors against OST of pathogenic *Campylobacter* species and to prevent their colonization.

Fig. 1A: Comparison of OST catalyzed N-linked glycosylation in bacteria and eukaryotes. Fig. 1B: The main source of *Campylobacter jejuni* infection in humans is through chicken as pathogen carrier (Picture adapted from Young, K.T. et al. Nat Rev Microbiol, 2007, 5: 665-679).

Invention

The three-dimensional structure of OST (PglB) from *C. lari* provides the first atomic model of acceptor sequon recognition and reveals a catalytic site that is formed by the transmembrane domain of the protein. Due to a bound substrate peptide, the model can be used to identify peptide-enzyme interactions enabling an alteration of the substrate specificity of OST. Engineering of OST will not only allow to glycosylate eukaryotic glycoproteins in bacteria (Fig. 1A), but can also result in the development of novel polypeptide acceptors with distinct properties. Based on the insight into the catalytic site, the model provides an opportunity to modify and tune the catalytic activity of OST. On the other hand it allows engineering of the oligosaccharide binding site in a way that OST can transfer eukaryotic type of glycans (Fig. 1A) or a novel kind of glycan.

The second part of the invention implies the three dimensional model of OST for identifying and designing new glycosylation inhibitors against pathogenic bacteria. Inhibition of N-linked glycosylation in *Campylobacter* will result in reduced colonization of chicken which is the main cause of gastrointestinal colitis worldwide (Fig. 1B).

Features & Benefits

The structure will enable:

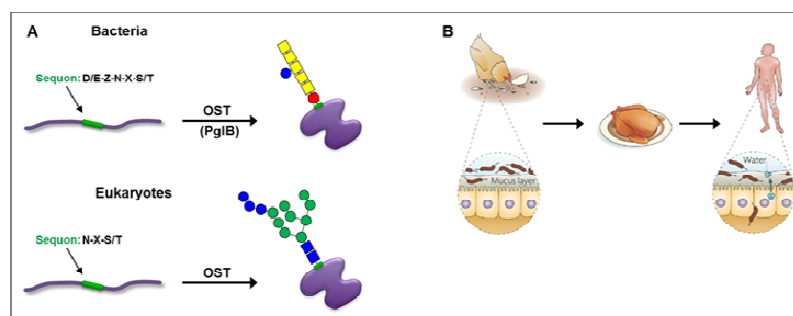
- Efficient and cost effective production of eukaryotic glycoconjugates in bacteria (*E. coli*, etc.)
- Increased efficiency of the OST enzyme activity by protein engineering of the OST binding site
- Allow the development and production of tailor-made glycoproteins
- Inhibition of N-glycosylation and therefore represents an efficient way to fight against pathogenic *Campylobacter* species

Field of Application

- Therapeutic glycoproteins - development and production of glycoconjugates in bacteria
- Veterinary applications - prevention of the human pathogen *Campylobacter* in chicken

References

- Lizak, C. et al. Nature, 2011, 474: 350-355



Ref. No. T-11-003

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