Structural Insights into GnT-I Substrate Recognition & Specificity

Roni D. Gordon[a], Prashanth Sivarajah[b], Malathy Satkunarajah[b], Dengbo Ma[b], Dragos Vizitiu[c], Chris A. Tarling[c], Stephen G. Withers[c], James M. Rini[b], *[a]Department of Biochemistry, University of Toronto. [b]Department of Medical Genetics, University of Toronto. [c]Department of Chemistry, University of British Columbia.* E-mail: roni.gordon@utoronto.ca

β-1,2-N-acetylglucosaminyltransferase I (GnT I; EC 2.4.1.101) is a key carbohydrate processing enzyme in the Golgi – it initiates the conversion of oligomannosyl to complex and hybrid N-linked glycans. GnT I, an inverting glycosyltransferase, catalyzes the addition of GlcNAc to the terminal 3-arm mannose of Man_5Gn_2 glycans found on glycoproteins in the secretory pathway.

We previously determined the x-ray crystal structure of the nucleotide-bound complex of GnT I in the presence of the native UDP-GlcNAc donor [1]. We now present a series of high-resolution donor analog complexes that provide insight into donor recognition and underscore the importance of the C2 position in catalysis.

We also report the structure of a ternary complex of both donor and acceptor substrates bound in the active site, which reveals how GnT I confers acceptor binding specificity by means of multiple subsites on the oligosaccharide.

[1] Unligil U.M., Zhou S., Yuwaraj S., Sarkar M., Schachter H., Rini J.M., *EMBO J.*, 2000, **19**, 5269.

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