

STRUCTURAL AND FUNCTIONAL ASPECTS OF GLYCOSYLTRANSFERASES

Christelle Breton

*CERMAV-CNRS (affiliated with Université Joseph Fourier), Glycobiologie
Moléculaire, BP53X, F-38040 Grenoble cedex 9, France*

Glycosyltransferases (GTs) constitute a large family of enzymes that are involved in the biosynthesis of oligosaccharides and polysaccharides. These molecules of fascinating diversity mediate a wide range of functions from structure and storage to signalling. Particularly, the carbohydrate moieties of glycoconjugates are mediators of biological information, playing roles in cancer, infection, immunity, and so on. Aberrant glycosylation is a hallmark of the malignant phenotype.

The glycosyltransferases transfer a sugar residue from an activated donor substrate, usually a nucleotide sugar donor, to an acceptor that may be a protein, a lipid or a growing oligosaccharide, and they generally display exquisite specificity for both the glycosyl donor and the acceptor substrates. In eukaryotes, most of GTs are resident membrane proteins of the endoplasmic reticulum and the Golgi apparatus. Golgi-resident GTs are those that received the most attention because they are responsible for the synthesis of complex glycans attached to proteins and lipids (the so-called glycoconjugates).

The analysis of the wealth of sequences that are now available in databases allowed the classification of glycosyltransferases in a large number of families on the basis of sequence similarities. In contrast, this enzyme family is characterized by a more conserved 3D architecture. Only a limited number of crystal structures is currently available but homology modelling can help to decipher structure-function relationships of this class of enzymes [1]. This approach may help for rationalizing experimental data and designing inhibitors that would be of interest as therapeutical compounds. With the huge amount of data coming from the large-scale sequencing project, the need for appropriate computational tools to identify and retrieve all glycosyltransferase sequences is becoming more and more important [2]. Detection of conserved peptide motifs that have a direct role in the functional aspects of glycosyltransferases is one approach to identify remote similarity [3]. With the availability of more crystal structures, the use of fold recognition methods is also very promising for identifying the folds of many GT families [4].

[1] Heissigerova *et al. Glycobiology* **2003**, *13*, 377-386

[2] Wimmerova *et al. Biochimie* **2003**, *85*, 691-700

[3] Chazalet *et al. J. Bacteriol.* **2001**, *183*, 7067-7075; Jeanneau *et al. J. Biol. Chem.* **2004**, *279*, 13461-13468

[4] Breton *et al. Biochem. Soc. Symp.*, **2002**, *69*, 23-32.