

## GLYCOSYLTRANSFERASES: WHAT WE THINK WE KNOW AND WHAT WE CERTAINLY DON'T KNOW

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On 01-June 2005, there were 14527 open-reading frames believed to encode activated-sugar dependent glycosyltransferases! Such a vast number of potential enzymes presents both challenge and opportunity. Whilst most mammalian glycobiochemists are aware of the specificities of their enzymes, in the bacterial and plant kingdoms the function of most open reading frames are certainly not known. In an attempt to use sequence as the common language to bridge this divide, the CAZy classification [1] places these ORFs into 78 sequence-based families. At the 3-D level structures have been reported for members of just seventeen of these families. We know that many of these structures share one of two common folds, termed GT-A or GT-B, with some structures [2] unusual variants of these. We know that, in recent evolutionary terms, there are both inverting and retaining enzymes with both global folds. We certainly don't know enough about glycosyltransferase reaction mechanisms. At a simplistic level inversion is understood whilst retention remains controversial. For neither configurational agenda do we understand the nature (shape and charge) of the transition-state, nor the conformational itineraries during catalysis (in marked contrast to glycoside hydrolysis [3], for example).

In this plenary lecture, I shall attempt to review the structural enzymology of glycosyltransferases covering the major fold types and configurational issues. In addition to 3-D structure and reaction mechanism, attention will be paid to high-throughput means for defining substrate specificity such as Ben Davis' "GAR" screening approach [4]. Examples will be drawn from both the wider literature and recent unpublished and "in press" data including a GDP-Mannosyltransferase [5].

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### References

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