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New frontiers in glycoconjugates

At the end of the IXth International Symposium on Glycoconjugates, the Chairmen of each session summarized the presented results and, on this basis, attempted to show the ways for the future of glycoconjugates. Their remarks are reported in the following series of papers.

The structure of glycoconjugates: a continuing challenge

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No other class of cell surface membrane constituents reflects the nature and the state of a living cell in such a general way as do the oligosaccharides of their glycosphingolipids. The systematics of the changes in structure which accompany differentiation and dedifferentiation attract more and more attention. Knowledge of the characteristics of the lipid, as well as the protein-linked oligosaccharides in relation to development and malignancy may ultimately be of diagnostic value. Information on the tumor-associated changes occurring in glycoproteins has been rather indirect, until recently. It has now been shown that besides structural changes in the periphery of the chain, important alterations may occur in the branching of the lactosamine-type asparagine-linked carbohydrates. This may be related to an ectopic expression of *N*-acetylglucosamine transferase III.

The basis for obtaining further insight into the exciting functions of glycoconjugates in biological the determination of the structure. In view of the immense problems in elucidating the primary structures of intact glycoconjugates, degradation to partial structures is usually the first step. In addition, the chemical procedures that have been developed for more or less specific breakdown of glycolipids and glycoproteins, the application of enzymes for cleaving carbohydrate chains from glycoproteins and glycolipids is becoming more feasible. The purification of PNGases as well as endoglycoceramidases marks a significant step forward. The next step is the separation of mixtures of carbohydrates. Significant progress has been made in the high pressure liquid chromatography separation of oligosaccharides. In particular, the introduction of a new pellicular strong anion–exchange resin seems very promising. Furthermore, the improvement of the detection levels down to the pmol range is important. The application of UV, absorbing ligands has also to be mentioned in this respect.

For the determination of the primary structure, miniaturization of methylation analysis is a relevant development. It makes feasible the analysis of glycoconjugates that are available only in minute amounts. Biochemical processes and alterations therein can probably be traced in this way. As a method for the analysis of oligosaccharides, mass-spectrometry (MS) is becoming increasingly important. In addition to the development of MS–MS, continuous flow FAB–MS has to be mentioned. ^{1}H NMR spectroscopy has attained a firm position among the various identification techniques. For compounds belonging to the family of known carbohydrate chains, 1-D methods based on the structural reporter group concept are usually sufficient. For new compounds or for carbohydrates bearing non-carbohydrate substituents, 2-D-techniques may be necessary. In several instances, the amount of material available may be a limiting factor in the application of sophisticated NMR techniques. Further improvement of the sensivity and resolution of ^{1}H NMR spectroscopy is urgently required.

Among the many new structures that have been revealed, the phosphatidyl inositol anchor occurring in biomembranes deserves special attention.

Important future aims in the structural analysis of glycoconjugates include improvements in the analytical methods and sensitivity of the techniques used. Furthermore, the conformation of glycans in solution needs to be more closely evaluated. The spatial structure of intact glycoconjugates is especially relevant. For an understanding of interaction and recognition processes, it is necessary to know which part of the carbohydrate is oriented to the outside. The development of methods that allow the study of the interac-

tion with complementary compounds at the molecular level is also needed. For the study of homogeneous 'crystalline' glycoconjugates, the application of X-ray analysis at low temperature may lead to a further understanding of the interaction between glycan and aglycan. Theoretical calculations and molecular modelling should be emphasized as techniques that are indispensable additional tools.

To summarize: a further sophistication of the methods of determining the primary and spatial structure of the carbohydrate moieties of glycoconjugates may contribute significantly to gaining insight into fundamental aspects of cell–cell interaction, cell differentiation, tumor-associated alterations and the interaction between cells and macromolecules.