
Preface

As the number of -omics words proliferate in the analytical life sciences, glycomics is a word increasingly being used as biological researchers realize that carbohydrates may significantly contribute to the functional diversity in the cell. So what is in a word? Glycomics uses the chemical prefix for a sugar, “glyco-”, and follows the naming convention established by genomics (which deals with genes) and proteomics (which deals with proteins). If we define *glycome* as the glycan complement of the cell or tissue as expressed by a genome in time and space, then glycomics is the analysis of the structure and function of these glycans or oligosaccharides (chains of sugars) attached to biomolecules. By this definition, the field includes the analysis of glycoproteins, proteoglycans, glycolipids, peptidoglycans, and lipopolysaccharides. *Glycoproteomics*, the study of the glycome attached to proteins, is gaining increasing interest on the back of the proteomics revolution as it becomes obvious that many of the changes associated with disease and differentiation are due to the modifications to the proteins rather than only to the regulation of the expression of the gene.

Historically, the main difficulty which has slowed the understanding of the biological role of glycans has been the perception that the analysis of sugars is too hard and is best left to the experts in the field. This book tries to remedy this misconception as there is an increasing availability of sample preparation, chromatographic, electrophoretic, mass spectrometric, and bioinformatic tools specifically designed for the analysis of glycosylation. In addition, approaches to investigate the interaction between these glycans and a variety of carbohydrate-recognizing proteins are presented so that the functional significance of the oligosaccharides can be explored. We have assembled the experts in the field, and this book presents a compendium of detailed protocols that they use routinely in their laboratories. The methods described can all be readily implemented using the current technologies already in use in research laboratories, especially those established for proteomics research.

The protocols in **Sect. I** concentrate on glycoprotein and proteoglycan analysis and include different approaches to determine the structure of both the N-linked and O-linked glycans released from glycoproteins and the glycosaminoglycans (GAGS) released from proteoglycans (**Subsect. A**). With the limiting quantities of biological material, as in proteomics, mass spectrometry has emerged as the detector of choice for glycan analysis and a wide variety of sample preparation, derivatization, chromatography, and mass spectrometric techniques are currently being used. We have included some methods which may be similar in principle but which differ in their implementation in the different author's laboratories. Current glycomic analytical methods have evolved based on available instrumentation, and a selection of protocols is provided here for the suite of instruments already existing in research laboratories that want to go down the glycomics path without investment in expensive new instrumentation. In much the same way as kitchen recipes, the reader can choose which detailed method works best “in their hands”!

Some glycosylation site determination methods are also described (**Subsect. B**) and usually involve enrichment of the glycoprotein or glycopeptide before analysis by mass

spectrometry. The “holy grail” of glycoanalysis is to be able to characterize the oligosaccharide heterogeneity at each glycosylation site on a protein or proteoglycan — this has not yet been achieved by a generic approach. A separate section (**Subsect. C**) reviews the current practices used for the analysis of the specific single O-GlcNAc found on nuclear and cytoplasmic proteins.

As in proteomics, the development of bioinformatic tools for the analysis of the mass spectrometric data holds the key for widespread adoption of the challenge of glycan analysis (**Subsect. D**). Many of the software tools available for the analysis of proteomics data have the potential to be adapted for use in glycomics research and the development and adoption of these tools will enable high-throughput glycomics analysis to be carried out. At this point, we would like to acknowledge the significant contribution to the area of glycoinformatics of one of our authors, Dr. Claus-Wilhelm (Willi) von der Lieth, who unexpectedly passed away on November 24, 2007. Dr. von der Lieth, of the German Cancer Research Center, Molecular Structure Analysis Group in Heidelberg, was a global leader in the development of informatics systems for glycobiology and was the inspiration behind the EUROCarbDB project. His vision, coupled with his enthusiasm, professional and personal skills, will be sadly missed.

Of course, the reason for carrying out the analysis of what and where glycans are in the cell is so the researcher can ultimately determine what they do. Methods for measuring their diverse biomolecular interactions are described in **Sect. II** and cover glycan arrays, mass spectrometry, NMR, antibodies, and small molecule inhibitors.

As more experimenters take up the challenge of glycan analysis, and as more technologies are developed and used, we are confident that the results obtained will provide valuable insights into the biology of cell-cell communication and interaction. It seems that whenever we perturb the cell a change in glycosylation occurs — the function of these changes is largely unknown and tantalizes the researcher, but it is our belief that the more is known about the structure and function of these ubiquitous molecules the closer we will get to the understanding of the complexity of the glycome and its part in the complexity of biology. We hope that this book, *Glycomics: Methods and Protocols*, contributes to this goal, and we sincerely thank all the contributors for sharing their knowledge with the wider community in such a detailed and explanatory format.

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Glycomics

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