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# Preface

The mucins (mucus glycoproteins) have long been a complex corner of glycoprotein biology. While dramatic advances in the separation, structural analysis, biosynthesis, and degradation have marked the progress in general glycoprotein understanding, the mucins have lagged behind. The reasons for this lack of progress have always been clear and are only now being resolved. The mucins are very large molecules; they are difficult to separate from other molecules present in mucosal secretions or membranes; they are often degraded owing to natural protective functions or to isolation methodology and their peptide and oligosaccharide structures are varied and complex. Understanding these molecules has demanded progress in several major areas. Isolation techniques that protect the intact mucins and allow dissociation from other adsorbed but discrete molecules needed to be developed and accepted by all researchers in the field. Improved methods for the study of very large molecules with regard to their aggregation and polymerization were also needed. Structural analysis of the peptide domains and the multitude of oligosaccharide chains was required for smaller sample sizes, for multiple samples, and in shorter time. In view of these problems it is perhaps not surprising that the mucins have remained a dilemma, of obvious biological importance and interest, but very difficult to analyze.

The driving force behind the production of *Glycoprotein Methods and Protocols: The Mucins* has been the accumulation of novel advances in the ability to analyze mucins reliably and the impact of molecular biology and immunology on the general awareness of mucins as important molecules. This volume is overdue as there is no comprehensive compendium of methods for mucin analysis. It is vital to gather together protocols from those groups who have sorted out the fundamental methods in order that others wanting to use these advances have a reference to follow. In this way *Glycoprotein Methods and Protocols: The Mucins* will make a major contribution in eliminating variation between individual labs and enable the mucin field as a whole to make genuine comparative studies. The range of analytical techniques presented here represents the culmination of the recent advances in the mucin field alluded to above. In several cases this is the result of many years' continuous struggle and it is very satisfying to bring together these new methods in one volume.

The initial problems of mucin analysis were related directly to their purification from secretions and tissues. These methods have been refined to include extraction in denaturing solvents, protection with antiproteolytic agents, and combinations of repeated density gradient centrifugation, gel filtration, ion-exchange chromatography, and electrophoresis, especially in agarose gels (Chaps. 1, 2, 7, and 8). Parallel to these developments have been the efforts to detect and quantify mucins in tissues and in extracts during purification (Chaps. 3–6, 29, and 30); this is still a growing area.

Much of the current knowledge of mucin polypeptide structure has been derived from direct peptide analysis and sequencing (Chaps. 10–13). Confirmation of much of these data and considerably more information with regard to molecular organization and tissue-specific expression patterns has been derived from the molecular biological description of mucin genes (Chaps. 24–28). This has led to the identification of mucin domains, variable number tandem repeat sequences, and new proposals for the way in which mucins are assembled and for their tissue-specific function.

In keeping with the high proportion of carbohydrate typically present in mucins, the latest sensitive methods for the total monosaccharide composition and sequence determination of oligosaccharides is covered (Chaps. 14–16). This is often a large undertaking since the number of individual oligosaccharide chains in a purified mucin is often high (i.e., at least 20–50 structures). Further modifications of the oligosaccharide chains are also common, especially sulfation (Chap. 17), and these additions present their own analytical problems.

The biosynthesis of mucins has been studied in a variety of tissue and cell culture systems. The new developments in separation and mucin gene structure have focused the direction of this work on the design of new specific reagents (Chaps. 18–21). In addition, the glycosylation and sulfation reactions and their inhibition have opened new concepts in the approach to mucin carbohydrate biology (Chaps. 22 and 23).

Study of the degradation of mucins has been hampered by the limited availability of suitable mucin-related substrates. This is still an area of development, one that has benefited from the new information appearing on the detailed structure and organization of the mucins. The concept of a whole “mucinase” activity is also addressed in this volume (Chap. 31) and is backed up by a more detailed consideration of the known members of the total mucin degrading activity (Chaps. 32–34).

One of the most exciting and novel aspects of mucin biology to appear in the last few years has been the interaction of mucins with organisms. This volume would not be complete without these novel concepts concerning bacte-

rial interaction in biofilms (Chap. 36) and the general interactions of bacteria with mucins (Chap. 35).

The cellular and humoral responses to mucins (largely MUC1) has proved to be a major item of interest in cancer biology. As a result it is appropriate that representation of this methodology is also part of the volume (Chaps. 37–41).

The compilation of this practical handbook has been made easier by the trouble taken by the authors to fit their protocols to the format. This volume represents a start in the collection of a reliable and comprehensive collection of methods for the mucin researcher.

***Anthony P. Corfield***



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