Preface

"L'esperienza de questa dolce vita."
The experience of this sweet life.

Dante Alighieri, *La Divina Commedia, Paradiso*, Canto XIX

Many of us remember when complex carbohydrates were viewed by most scientists simply as nuisances whose structures were hopelessly complicated and whose functions at best were obscure. Arguments were made that cells synthesized their glycans more for sport or even "decoration" than for necessity, and that differences in glycan structures between cells might be epigenetic irrelevancies, rather than genetically controlled essentials. If Dante had been a scientist in the latter part of the twentieth century, he surely would have assigned a level in his *Inferno* to those who found themselves mired in understanding glycan structure and function, and who understood well the warning at *Inferno's* entrance, "Abandon hope all ye who enter." With the shrinking number of open reading frames (ORFs) identifiable in genomes from humans to yeast, however, no one would now hypothesize that a cell makes a protein or any product, especially those made by the action of several proteins within a pathway, which serves no particular function. Thus, with new times comes new knowledge; surely now Dante would have the glycoscientists ascend to *Paradiso* to join the anointed ones.

The list of recent discoveries showing critical functions of glycans is impressive:

- Regulation of lysosomal enzyme biosynthesis and the roles of glycosylation in molecular targeting
- Regulation of the initial steps of the inflammatory response and leukocyte adhesion and turnover, as well as lymphocyte homing
- Mediation of the recognition and infection by many pathogens, including HIV, via dendritic cell lectins
- Identification of the family of congenital disorders of glycosylation that cause birth defects
- Demonstration that mutations in glycosyltransferases cause a form of muscular dystrophy known as the muscle–eye–brain disease
- A Ser/Thr modification by *N*-acetylglucosamine, *O*-linked GlcNAc, serves to regulate diverse signaling pathways, from transcription factor binding to insulin resistance
- Understanding that protein *N*-glycosylation fundamentally controls glycoprotein quality control and biosynthesis in the endoplasmic reticulum/Golgi apparatus
- Multiple activities of glycosaminoglycans, including heparan sulfate, regulate cell signaling and angiogenesis, as well as blood clotting

- Glycans are recognized by antigen-presenting cells, including macrophages and dendritic cells, via numerous glycan-binding proteins that regulate immune responses
- Sialic acid-binding proteins in leukocytes control cellular differentiation.

Moreover, throughout the field of glycoscience there is excitement and anticipation because new glycan functions are constantly being discovered.

All of these biological processes are controlled by specific glycan structures that are biosynthetically regulated and that are often recognized by specific glycan-binding proteins or lectins. A scientific hallmark of the first part of the twenty-first century, therefore, has been the development of technologies and methodologies to identify the details of post-translational modifications, in particular glycan structures, thus accelerating the pace of discovery of glycan function. These accomplishments have led to the establishment of glycomics as one of the fundamental areas of biological and biochemical study, and the ambitious goal of defining human and animal glycomes as one of the twenty-first century's most important quests. The definition of glycomics used in this book is very broad, encompassing all those molecules that contain glycans and which regulate or whose structure and function are regulated by glycans. Thus, this quest to understand the glycome is extraordinarily challenging, since it requires an understanding of both glycan structures and the molecules to which glycans are linked, and requires defining their altered expression in different cells during development and disease.

The *Handbook of Glycomics* contains descriptions of state-of-the-art technologies that are in current use to describe and quantify changes in glycomes, as well as the application of these technologies to the study of specific organisms, cells, and diseases. For a comprehensive background on glycobiology and glycoscience, readers are referred to the *Essentials of Glycobiology,* 2nd edition, 2009, Cold Spring Harbor Press.

The chapters in the *Handbook of Glycomics* were written by experts in the field with experience in studying glycan structures using newly developed methods for the analysis of many different types of glycoconjugates, including glycoproteins, glycolipids, and glycosaminoglycans/proteoglycans. Moreover, these authors are involved in integrating this knowledge into a systems approach to the field, incorporating glycan structure, gene expression, and glycobioinformatics to propel our understanding of the functions of glycans in physiology, development, and disease. The book is organized into six sections. In Section I, Glycoconjugate Structural Analysis, Meschref and Novotny describe *N*-glycan analysis and Wells describes *O*-glycan analysis using a glycoproteomics approach. The complex nature of glycosaminoglycan structural analysis is addressed by Zhang, Zhang, and Linhardt. In Section II on Glycotranscriptomics, the use of isotope labeling approaches to aid in mass spectrometry of glycans and the rapid identification of structural differences of glycans compared between different sources are described by Cummings and Smith. Then Nairn and Moremen describe the approaches used to analyze transcription of genes that regulate and recognize the glycomes. In Section III, Protein–Glycan Interactions, Smith and Cummings describe the use of glycan microarrays to identify glycan recognition by glycan-binding proteins and lectins, and Hirabayashi describes how chromatographic and mass spectrometric techniques are used to define glycan–protein interactions. Section IV, Glycobioinformatics, includes chapters by York, Kochut, and Miller on integrating glycomic information and databases, and by Hashimoto and Kanehisa on the development and use of the KEGG GLYCAN for integrating biosynthetic pathways, genetics, and glycan structures. Ranzinger, Herget, Lütteke, and Frank describe the European Glycomics Portal, which promotes integration of glycan-related data from many sources. Section V gives overviews of different glycomes and their relationships to functional glycomics and immunity, as described by Redelinghuys and Crocker in relation to the mouse and human immune systems; North, Chalabi, Sutton-Smith, Dell, and Haslam in regard to humans and mice; Sharrow, Aoki, Baas, Porterfield, and Tiemeyer in *Drosophila*; Davidson in malaria;

and van Die and Cummings in parasitic worms. The final section of the book, Section VI, is on Disease Glycomics, where cancer glycomics is discussed by Pierce, and glycans in human disorders of glycosylation are discussed by Freeze and Eklund.

The *Handbook of Glycomics* serves as a portal to these broad subjects on glycomics, since the field is expanding at a stunning pace, with information pouring in daily on glycomes, glycan-binding proteins, enzymes (glycosyltransferases and glycosidases), and transporters in microbes, parasites, plants, and animals. There are clearly many areas of research on glycomics that will need to be included in updated editions of the *Handbook*. The techniques and conceptual approaches described in this edition of the *Handbook of Glycomics* will no doubt be a valuable reference in this field for years to come, and will provide the interested reader both depth and diversity in this rapidly expanding and exciting component of biology.

We are indebted to those who have helped make this book possible, including the many authors who graciously responded to our requests and cajoling, along with the expert staff at Elsevier, including acquisitions editor Christine Masahina and developmental editor Rogue Schindler.

The most beautiful experience we can have is the mysterious.

—Albert Einstein

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