Preface

The clinical applications of insulin and the glycosaminoglycan-based drug heparin in the early 20th century mark the dawn of modern medicine. However, they are quickly overshadowed by the small molecule-based drugs. Heparin might not be approved as a drug if the clinical trials were conducted in the 21st century. As a biological drug isolated from animal tissues, heparin has not only structural variations but also many biological functions beyond the one drug–one target concept of modern medicine. Chemical modification of heparin can enhance its conceptual anticoagulant activity in vitro but such modified heparin activates the contact system in vivo, which was associated with hundreds of anaphylactic reactions and at least 149 anaphylactic reaction-associated deaths in the United States in 2007 and 2008. Through trial and error, the structure-defined modern drug or a combination of them cannot have the life-saving property offered by heparin. Insulin, on the other hand, is one of the few proteins in blood circulation that is not glycosylated. Type 2 diabetes is mainly caused by insulin resistance. It turns out human insulin receptor is a heavily glycosylated protein and abnormal glycan structures assembled on the insulin receptor contribute to the failing insulin/insulin receptor signaling. Thus, both glycan-based drugs and glycosylations remain to be the "dark matter" of the biological universe.

Glycan-based biomarker studies presented in Part A of this book series indicate that cancers and other complex diseases are associated with systems malfunction. Tumors might be the result but not the cause of the systems malfunction, which suggests that both tumor and systems malfunction had to be treated simultaneously to achieve better care of patients. Multiple targets or system approach in treating diseases is a well-accepted concept in traditional Chinese medicine. The polypharmacology and multicompositions of glycan-based drugs are similar to traditional Chinese medicine. As a consequence, more than a dozen of glycan-based drugs have been approved by the Chinese FDA during the past 40 years. Most of them are used as adjuvant drug during chemo- or radiation therapy for cancer patients. All glycan-based drugs show multiple health-promoting effects including immunomodulation, antitumor, antiaging, antioxidation, hypoglycemic, hypolipidemic, antiradiation activities. The sulfated glycan-based drugs show additional anticoagulant, antiviral, and antimetastatic effects

through high-affinity interactions with a variety of proteases, protease inhibitors, chemokines, cytokines, growth factors, and their respective receptors.

Part B of this book series is focused on the clinical effects of the glycan-based therapeutics. We discussed the heparin, eight different types of low molecular weight heparin, synthetic heparin pentasaccharide Fondaparinux, and heparinoids Danaparoid and Sulodexide from Chapters 1–4 sequentially. The heparin derivatives only represent a refined use of heparin and none of them matches the polypharmacology of heparin. Marine glycan-based drugs are presented in Chapters 6–8. Among them, heparinoid PSS is an anticoagulant and antithrombosis drug that can be taken orally, which is advantageous over the injection-required heparin. The eight fungal glycan-based drugs are presented from Chapters 8–16. The preclinical studies of polysaccharides from traditional Chinese herbs are deliberated in Chapter 17. Glycan- and glycosaminoglycan-based nutraceuticals are discussed in Chapter 18. The importance of correct glycosylation in monoclonal antibody-based drugs is addressed in Chapter 19. Last but not the least, the glycosylated small molecule drugs that are widely used as antibiotics, antitumor, antidiabetes, and other drugs are summarized in Chapter 20.

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