Preface

Glycosylation is a ubiquitous and important modification of biological molecules, particularly of proteins (glycoproteins). Although glycosylation pathways have been elucidated and the structures of the carbohydrate moieties that decorate numerous glycoproteins have been characterized, the contribution of glycosylation to protein structure and function for many viral glycoproteins is not fully understood. The latter applies particularly to the surface envelope glycoprotein spike of HIV-1.

HIV, like many other viruses, takes advantage of cellular biosynthetic pathways for its own benefit. Roughly half of the molecular mass of the HIV envelope glycoprotein spike is contributed by glycans and large sections of the spike are covered densely by glycosylation. It has long been known that proper glycosylation is critically important for the proper folding of the HIV glycoprotein spike and, consequently, for viral infectivity. Not unlike other enveloped viruses, HIV also utilizes glycosylation as a means to protect vulnerable sites on its envelope glycoprotein from immune recognition; the attached glycans, assumed to be immunologically inert "self" molecules, were until recently considered a largely insurmountable challenge for antibody recognition. However, significant progress in recent years has led to a better understanding how glycans contribute to HIV's ability to infect and persist as well as the potential exploitation of HIV glycans as targets for the development of an effective HIV vaccine and possible virucides. It is within this context that this book is placed.

The emerging view is that the glycosylation profile of HIV strains is homogeneous overall but that each virus strain diminishes or increases the specific number and position of its glycans depending on the level of host immune pressure. At the same time, the recent identification of several glycan-specific and glycan-dependent HIV-neutralizing antibodies with exceptionally broad and potent activity has galvanized the HIV vaccine field, showing that at least some glycans on the virus form conserved "non-self" patches that represent extremely vulnerable targets for immune recognition. Molecular characterization of the epitopes of these antibodies shows that they recognize their carbohydrate epitopes in ways that were previously unimaginable. Such studies, together with those seeking to understand how glycosylation patterns influence the ontogeny of anti-HIV-neutralizing antibodies generally, will

likely inform strategies to design novel immunogens. The same epitopes may prove useful as targets for therapeutic agents such as lectins, an important aspect of microbicide development given HIV's insidious ability to corrupt innate immune cell patrols to gain access to CD4+ T cells in lymphoid and peripheral tissues.

This book comprises seven chapters that are meant to provide a view of recent advances in our understanding of the impact of HIV glycans in infection and their promise for immunological and therapeutic intervention. In selecting contributors for this book, I have tried to enlist several investigators, especially those at early career stages, who have been instrumental in moving research in this area of research forward. Although significant gaps remain in our knowledge of various aspects of HIV glycosylation, for example, understanding why HIV glycan patches are immunogenic during infection but apparently not so upon vaccination with current immunogens, it is clear that advances in the last several years have led to novel collaborations between glycobiologists and immunologists. The book as a whole is meant to give the reader an overview of the impact that cross-disciplinary research has had on the study of HIV glycans. I hope that this collective effort will serve as a comprehensive reference for researchers in the HIV field and particularly as an inspiration for newcomers to delve deeper into the role of HIV glycosylation in infection and immune interactions.

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