

Preface

Editor's Introduction

Although the utility of human antibodies as medical therapeutics for cancer and immune diseases has been well-established, it is only beginning to be realized for the treatment of viral infectious diseases. Polyclonal immunoglobulins have long been used for some viral diseases, but they have limited potency and disease scope. It should theoretically be possible to create monoclonal or oligoclonal antibody preparations that capture the essential curative functions of the humoral immune response to viral pathogens, yet only a single humanized monoclonal antibody (pavilizumab) has been approved as a viral countermeasure. Reliable technologies for creating human or humanized antibodies with defined viral antigen specificities are well-established. Accordingly, current antibody development efforts are focused on identifying and cloning the particular antibodies that contain the fundamental curative potency of the polyclonal humoral immune response.

The limited spectrum of available viral antibody therapeutics may be attributed, in part, to the unique technical challenges that each virus presents with regard to its life cycle, capacity for spontaneous mutation, and clinical manifestations. The articles in this volume address these issues from different perspectives. For instance, the clinical value of an antibody may depend on the genetic stability of the epitope it recognizes, the prevalence of that epitope in the viral population, the kinetics of the antibody/antigen interaction, the functional implications of epitope binding, and the interactions between the antibody and the immune system, which are often mediated by the Fc portion of the antibody. In some settings, a single antibody may be sufficient, whereas in others a combination of 2 or more may be preferred.

The articles in this volume have been selected to demonstrate the progress in the development of human antibody therapeutics for viral disease. Keck et al. review the nature of the immune response to the Hepatitis C virus (HCV) and the details of viral neutralization by antibodies, providing a conceptual model for the clinical use of HCV-specific antibodies. Huber et al. summarize the initial clinical experiences

with antibody therapeutics for Human Immunodeficiency Virus (HIV), which can be targeted to either the HIV virion or to host cell proteins. A discussion of the breadth immune strategies that is required to control human rabies is provided by Nagarajan et al., with a particular focus on India and other developing countries in which rabies is endemic. The development of pavilizumab for RSV prophylaxis is reviewed in Wu et al., in addition to results of antibody optimization studies that provide surprising insights and have broad general implications for anti-viral antibody engineering. Melhop and Diamond explicate the biology of West Nile Virus (WNV) as a general model for flaviviruses, while using their cloned antibodies as a springboard to consider the mechanisms of WNV neutralization. The volume concludes with a description of methods to clone human antibodies in their native configurations, which access a class of antibodies that differ from those obtained by recombinant DNA or transgenic mouse methods.

The articles in this volume are definitive and comprehensive reviews written by thought leaders who have sought to define the principles of viral neutralization by human antibodies. They explore and anticipate the obstacles and opportunities that will be encountered as the power of human antibodies is harnessed to address the vast, un-met need for effective anti-viral therapeutics.

Philadelphia, PA
March 2007

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Human Antibody Therapeutics For Viral Disease

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2008, XII, 190 p. 18 illus., 7 illus. in color., Hardcover

ISBN: 978-3-540-72144-4