Preface

Monoclonal antibodies have become a key therapeutic modality for a broad range of diseases. The therapeutic potential of monoclonal antibodies is derived from their exquisite specificity and high affinity binding to their antigen target. The therapeutic utility of monoclonal antibodies was quickly realized after the development of hybridoma technology by Kohler and Milstein in 1975.

The first generation of therapeutic antibodies was of murine origin. These antibodies were of limited therapeutic value because patients who received these agents developed an immune response to the mouse protein, referred to as human anti-mouse antibody (HAMA) response. HAMA responses negatively impacted the efficacy of antibodies of murine origin; this limitation fostered the development of new antibody technologies to reduce the immunogenicity of murine antibodies by making them more human-like. These technologies, employing recombinant DNA methods, led to the development of chimeric antibodies; chimeric antbodies maintain the murine variable region linked to human constant regions and retain approximately 35% of murine protein sequences. Additional improvements in recombinant DNA technology led to the development of humanized antibodies, which retain about 5–10% of murine protein sequences.

With further advances in antibody technology, two major platforms are now employed to generate fully human monoclonal antibodies. One platform relies on display technologies, namely phage, ribosomes, or yeast that display human antibody variable regions. The second major platform relies on transgenic mice that have been genetically engineered to produce human antibodies.

A direct consequence of the above-described technological advances has been a significant investment on the part of the biotechnology and pharmaceutical industry to develop antibodies and an exponential growth in the therapeutic market for these agents. Moreover, several therapeutic monoclonal antibodies have attained blockbuster status with sales exceeding the billion-dollar mark and beyond.

Despite the exponential growth in the therapeutic market of monoclonal antibodies, it is also important to note that there still remains a considerable unmet medical need in the three main areas of study for investigational human

monoclonal antibodies: cancer, immunological, and infectious diseases. It is expected that therapeutic monoclonal antibodies will provide valuable new treatment options for these diseases.

The main objective of this volume is to provide a comprehensive overview of the translational considerations for developing antibody-based therapeutics from discovery to the clinic. The initiating event that ultimately led to the publication of this endeavor originated from a perennial annual short course at the Protein Engineering Summit (PEGS) that we introduced in 2008 and still teach currently. From our experiences with this course, we realized that many scientists, both in the academic and biotechnology/pharmaceutical community, do not possess in-depth knowledge of all aspects of antibody drug discovery and development; we therefore concluded a more formal and thorough discussion was warranted.

The topics covered have been carefully selected. Each chapter focuses on a specific aspect of translational strategies during the development of antibody-based therapeutics. Although some topics may not appear to be directly concerned with translational considerations or are technical in nature, addressing the ancillary aspects of antibody drug discovery and development should provide the reader with a broader understanding of the strategies involved in the drug development process of these agents. We envision that someone who has little if any current knowledge about therapeutic antibodies will be able to read this book and glean substantial insights from leading scientists across a broad range of expertise.

We are indebted to our many colleagues for their contributions to this endeavor.