Preface

More than ever, antibodies are being recognized as a major drug modality in a variety of diseases, including cancer, autoimmune diseases, infectious diseases, or even neurodegenerative disorders. Over 30 therapeutic antibodies have been approved, and novel molecules are entering clinical trials at an average rate of 50 per year that is predicted to continue well into the future. Huge improvements and breakthroughs have been necessary to achieve these impressive results. Therapeutic antibodies first entered clinical studies in the early 1980s, soon after the description of the original hybridoma technology by Kohler and Milstein, but most clinical studies led to disappointments. Major improvements were first needed in terms of safety and efficacy for these molecules to become efficient drugs. Advances in antibody engineering were instrumental at this stage and led to the production of chimeric, humanized, and finally human antibodies characterized by a much lower immunogenicity and the potential to interact more efficiently with effector cells of the immune system, including T and NK cells. This generation of antibodies has yielded major commercial and therapeutic successes, such as Trastuzumab, Rituximab, or Bevacizumab. These molecules have helped to establish the concept of therapeutic antibodies as one of the major avenues in targeted therapies. Notwithstanding these achievements, there is still a lot of space for improvements for these molecules in terms of activity, and a plethora of approaches have been attempted to optimize these molecules. Several techniques have been developed to tune the interaction of these antibodies with their antigens on one side, and with immune receptors on the other side, leading to stronger effector cell activation or to the modulation of the antibody half-life in patients. The classical architecture of the antibody molecule is bearing some inherent limitations, and many innovative formats have been proposed to overcome these major hurdles, by modulating the size, the valency, and the (multi)specificity of the original molecules.

Today, the visionary immunologist Paul Ehrlich himself would probably be amazed to discover the new possibilities offered by these "magic bullets" and all their derivatives.

This handbook was designed to give complete and easy access to a variety of antibody engineering techniques, starting from the creation of antibody repertoires and efficient ways to select binders from these repertoires, to their production in various hosts, their detailed characterization using various well-established techniques, and to the modification and optimization of these lead molecules in terms of binding activity, specificity, size, shape, and more. This book represents a direct access to the toolbox that antibody engineers need today to create the powerful molecules of tomorrow. This large collection of state-of-the-art antibody engineering techniques will be an invaluable resource for both experts and those new in the field, and most of all a source of inspiration to create the antibodies of tomorrow.

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