

FUSION PROTEIN TECHNOLOGIES FOR BIOPHARMACEUTICALS

APPLICATIONS AND CHALLENGES

EDITED BY STEFAN R. SCHMIDT

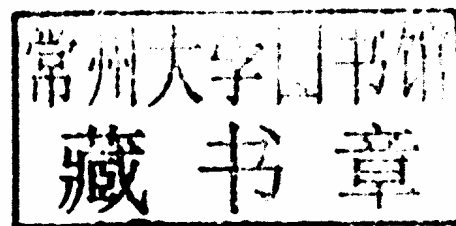
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PREFACE

This book covers the applications and challenges of fusion proteins; a relatively new class of therapeutic molecules. It is written both for experienced scientists wanting to acquire a deeper understanding of the underlying principles of fusion protein design and for students looking for a comprehensive introduction to this topic. This book shall serve as a source of inspiration by describing a wide range of examples. It gives an overview on the current state of the art and summarizes the huge potential of fusion protein design and functionality. The fascination of fusion proteins is derived from the vast range of possibilities that can be generated by joining individual natural molecules through human creativity. Overall, the rise of fusion proteins is driven by the revolution of genetic engineering, the improved knowledge on protein function, and the unmet medical need of many indications.

One of the many objectives is trying to fulfil the promise of Paul Ehrlich's *Magic Bullet*. This book also picks up the current trend of designing next generation biopharmaceuticals to enable combination therapy by addressing two targets simultaneously. Fusion proteins offer an elegant solution to the challenge of delivering equivalent concentrations of two active molecules to a specific location while keeping manufacturing costs low.

Inspiring the design and therapeutic applications of fusion proteins is the goal of this book. In the first few chapters, the readers are introduced to the concept of fusion proteins while some challenges such as immunogenicity are addressed. The main body contains three large sections on typical paradigms such as strategies to extend the plasma half-life, the design of toxic proteins, and finally utilizing fusion proteins for highly specific targeting. Each of these sections is preceded by an introduction summarizing the respective topic. The last part of the book covers novel

concepts including examples of highly relevant multi-functional antibodies. I have tried to maintain a balance between well-established molecules with clinical data and more experimental approaches that nevertheless appear very promising. All chapters are authored by experts in the field who happily share their deep understanding with the readers.

Throughout my professional life I have been studying proteins, starting with proteins whose malfunction causes disease and moving to monoclonal antibodies; always dealing with their isolation and characterization. My particular personal interest in fusion proteins was stimulated years ago when trying to optimize the half-life of an enzyme prototype. By digging deeper into the matter, I came across the many ways how to influence the plasma half-life. However, at this time no textbook about that topic was available, therefore, evaluating the different approaches was quite tedious. In the meantime, some books have been published addressing some isolated aspects that could be of interest to fusion proteins, but none really dedicated to fusion proteins in general. Identifying that gap, I started to collect material to prepare a focussed book and got into contact with several well-known colleagues working on various fusion proteins. Many stimulating discussions shaped the framework of the book. The result of these interactions is this book that covers all aspects of modern therapeutic fusion proteins.

I hope that my readers will enjoy reading this book as much as I enjoyed creating it together with so many talented people.

Finally I would like to thank my wife Gabriele and my son Felix for their encouragement and loving support.

STEFAN R. SCHMIDT

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