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## Preface

Since their introduction into the market over 20 years ago, biotherapeutics have constituted a large and growing percentage of the total pharmaceutical market, as well as approximately 25% of the R&D pipeline in industry. These biotherapeutics are having a huge global impact on the treatment of challenging and previously untreatable chronic disease. Currently biopharmaceuticals generate global revenues of \$163 billion, making up about 20% of the pharma market, and predicted to grow to over \$320 billion by 2020. The number of approved products in Europe and the USA has steadily increased to 2016 in 2014, of which 37 have “blockbuster” status, i.e., sales over \$1 billion per year, with monoclonal antibodies (Mabs) representing the most lucrative single product class [1]. Most significantly, nearly 50% of these biopharmaceutical products are produced in a single production host, i.e., Chinese hamster ovary (CHO) cells. Improving the efficiency of production of these biologics will be critical in controlling costs to healthcare systems as more of these drugs come to market.

There has been considerable success in developing high-producing CHO cell culture processes using approaches such as optimization of media formulation, improvements in expression vector design, and also improvements in the design of bioreactors. The next generation of improvements is expected to be made via genetic engineering of the host (CHO) cell itself to increase or decrease the expression of endogenous genes depending on the desired outcome, in order to improve the efficiency of the production of therapeutic protein product. In order to enhance the production capabilities and efficiency of the host cell line, an increased understanding of cellular physiology of CHO cells is of critical importance. There are substantial research efforts in progress focusing on the ‘omic analysis and systems biology of CHO cells to understand CHO cell physiology. The publication of the draft CHO-K1 genome in 2011 represented a major milestone in CHO systems biology. This information has been supplemented further with the publication of draft genomes for Chinese hamster and the CHO-S, CHO DG44 and CHO DXB11 cell lines. Availability of the genome sequence will facilitate the interpretation and analysis of transcriptomic and proteomic data to assess the physiological state of the cells under different growth and production systems. Combining all levels of regulation through systems biology models will unveil the underlying complexity inherent in CHO cell biology and will ultimately enhance and accelerate CHO productive capabilities in the coming decades.

This book includes reviews and protocols for genetic manipulation of CHO cells for recombinant protein production, including “difficult-to-express” therapeutics. A method is also included on the use of the recently described genome editing tool, CRISPR/Cas9, and how this can be applied to CHO cells. The book also includes a review and protocols for characterization of CHO cells using ‘omic approaches and how these methods can be used to improve efficiency of recombinant protein production during cell line development. Analytical methods for characterization of recombinant protein product, such as glycosylation and host cell protein analysis, are also described in this book.

I am deeply grateful to all authors for giving up their valuable time and for contributing to the book. I would also like to thank the series editor, Prof. John Walker, for help and guidance during the process of getting the book to publication.

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## **Reference**

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