

Therapeutic Proteins

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Methods and Protocols

Edited by

C. Mark Smales

*Protein Science Group, Department of Biosciences,
University of Kent, Canterbury, Kent, UK*

and

David C. James

*School of Engineering, University of Queensland, St. Lucia,
Queensland, Australia*

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Preface

With the recent completion of the sequencing of the human genome, it is widely anticipated that the number of potential new protein drugs and targets will escalate at an even greater rate than that observed in recent years. However, identification of a potential target is only part of the process in developing these new next generation protein-based “drugs” that are increasingly being used to treat human disease. Once a potential protein drug has been identified, the next rate-limiting step on the road to development is the production of sufficient authentic material for testing, characterization, clinical trials, and so on. If a protein drug does actually make it through this lengthy and costly process, methodology that allows the production of the protein on a scale large enough to meet demand must be implemented. Furthermore, large-scale production must not compromise the authenticity of the final product. It is also necessary to have robust methods for the purification, characterization, viral inactivation and continued testing of the authenticity of the final protein product and to be able to formulate it in a manner that retains both its biological activity and lends itself to easy administration.

Therapeutic Proteins: Methods and Protocols covers all aspects of protein drug production downstream of the discovery stage. This volume contains contributions from leaders in the field of therapeutic protein expression, purification, characterization, formulation, and viral inactivation. The contributors are all based at highly esteemed industrial and academic institutions from around the world and contact details are provided if researchers wish to obtain further information from the authors.

This book contains complete protocols set out in a simple step-by-step manner. It opens with an introductory chapter that discusses where therapeutic protein expression and downstream processing currently stand in terms of production, and contains thoughts on the direction of future developments from experts in the field. All other chapters contain a useful introduction describing the theory and background to the method, which is then followed by a list of all equipment and materials required to complete the protocol. The Methods section describes every step of the protocol and is cross-referenced to a Notes section that describes possible difficulties or problems that may arise, alternative methods and invaluable hints.

Therapeutic Proteins: Methods and Protocols includes protocols for the production of therapeutic proteins using a variety of sources, including bacterial and yeast expression systems and insect and mammalian cells. Methods for the purification of the resulting protein product are also described, as are purification protocols for the more traditional methods of preparing therapeutic proteins such as those sourced from plasma. Protocols for the characterization of therapeutic proteins throughout the pro-

duction process are described, along with viral inactivation and protein formulation methods and strategies. The book contains both general methods and information and specific case studies highlighting particular expression systems, proteins of interest or characterization procedures that may be equally applicable to other systems or recombinant proteins.

A large number of people have helped to put this book together so that it ultimately provides an invaluable resource to all those working in the field of therapeutic protein production. I would especially like to thank all the contributors whom have all made many excellent suggestions, and indeed, improvements, to this book. I must also thank John Walker, the series editor, for asking me to edit this book, and for his help and advice in preparing the final product. Thanks also to those at Humana Press who have helped put this together. Finally I would like to thank my co-editor David James for all his help and advice and my family for their support.

C. Mark Smales

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Contributors

- VARSHA BHAKTA • *Canadian Blood Services, Research and Development Department, Hamilton, Ontario, Canada*
- JOHN R. BIRCH • *Lonza Biologics plc, Slough, UK*
- ILSE BLUMENTALS • *Merck & Co., Inc., Rahway, NJ*
- INEKE G. A. BOS • *Department of Immunopathology, Sanquin Research at CLB, Amsterdam, The Netherlands*
- NICOLA BOSCHETTI • *R & D Virology, ZLB Behring AG, Bern, Switzerland*
- SHERI BRADSHAW • *Schering Plough Research Institute, Union, NJ*
- JOHN B. BRIGGS • *Department of Analytical Chemistry, Genentech Inc., South San Francisco, CA*
- LEE J. BYRNE • *Department of Biosciences, University of Kent, Canterbury, Kent, UK*
- MICHELE P. CALOS • *Department of Genetics, Stanford University School of Medicine, Stanford, CA*
- SUSAN CANNON-CARLSON • *Schering-Plough Research Institute, Union, NJ*
- JONG HYUN CHOI • *Department of Chemical and Biomolecular Engineering, Metabolic and Biomolecular Engineering National Research Laboratory, Bioinformatics Research Center, BioProcess Engineering Research Center, and Center for Ultramicrochemical Process Systems, Korea Advanced Institute of Science and Technology, Daejeon, South Korea*
- LILY CHU • *Merck & Co., Inc., Rahway, NJ*
- CONSTANCE CULLEN • *Schering Plough Research Institute, Union, NJ*
- COLLETTE CUTLER • *Schering-Plough Research Institute, Union, NJ*
- ARJO L. DE BOER • *Eukaryotic Microbiology, Groningen Biomolecular Sciences and Biotechnology Institute (GBB), University of Groningen, Haren, The Netherlands*
- ERIC C. DE BRUIN • *Department of Immunopathology, Sanquin Research at CLB, Amsterdam, The Netherlands*
- MARC DELORENZO • *Schering Plough Research Institute, Union, NJ*
- ERWIN DUITMAN • *Eukaryotic Microbiology, Groningen Biomolecular Sciences and Biotechnology Institute (GBB), University of Groningen, Haren, The Netherlands*
- ILARIA DURELLI • *Laboratory of Immunogenetics, Department of Genetics, Biology and Biochemistry, University of Torino Medical School, Turin, Italy and Research Center for Experimental Medicine (CeRMS), San Giovanni Battista Hospital, Turin, Italy*
- A. N. S. ESHWARI • *Product Development Cell, National Institute of Immunology, New Delhi, India*
- MARTIN FUSSENEGGER • *Institute for Chemical and BioEngineering, Swiss Federal Institute of Technology, ETH Zurich, Zurich, Switzerland*
- LALIT C. GARG • *Gene Regulation Laboratory, National Institute of Immunology, New Delhi, India*

- SABINE GEISSE • *Novartis Pharma Research CT/BMP, Basel, Switzerland*
- P. CLAYTON GOUGH • *Bioproduct Research and Development, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN*
- MICHAEL J. GRACE • *Schering Plough Research Institute, Union, NJ*
- C. ERIK HACK • *Departments of Immunopathology and Clinical Chemistry, Sanquin Research at CLB, VU Medical Centre, Amsterdam, The Netherlands*
- ALBERTO L. HORENSTEIN • *Laboratory of Immunogenetics, Department of Genetics, Biology and Biochemistry, University of Torino Medical School, Turin, Italy and Research Center for Experimental Medicine (CeRMS), San Giovanni Battista Hospital, Turin, Italy*
- MARK J. HOWARD • *Department of Biosciences, University of Kent, Canterbury, Kent, UK*
- LIHUA HUANG • *Bioproduct Research and Development, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN*
- KEN-ICHI IZUTSU • *National Institute of Health Sciences, Tokyo, Japan*
- DAVID C. JAMES • *School of Engineering, University of Queensland, St. Lucia, Queensland, Australia*
- MICHAEL A. JANKOWSKI • *Department of Characterization and Analytical Development, Wyeth BioPharma, Andover, MA*
- ZHENG JIN • *Institute for Cancer Research, College of Life Science and Technology, Xi'an Jiaotong University, Xi'an, Peoples Republic of China*
- ANNA JOHNSTON • *CSIRO Health Science, Parkville, Melbourne, Australia*
- ANDREW J. S. JONES • *Department of Analytical Chemistry, Genentech Inc., South San Francisco, CA*
- MARTIN JORDAN • *Laboratory of Cellular Biotechnology, SV-IGBB-LBTC, EPFL, Lausanne, Switzerland*
- RODNEY G. KECK • *Department of Analytical Chemistry, Genentech Inc., South San Francisco, CA*
- MARINA KORNEYEVA • *Bayer Corporation Biological Products, Clayton, NC*
- BEAT P. KRAMER • *Institute for Chemical and BioEngineering, Swiss Federal Institute of Technology, ETH Zurich, Zurich, Switzerland*
- BRITTANY LARKIN • *Schering-Plough Research Institute, Union, NJ*
- WENDY LAU • *Department of Analytical Chemistry, Genentech Inc., South San Francisco, CA*
- SANG JUN LEE • *Department of Chemical and Biomolecular Engineering and Center for Ultramicrochemical Process Systems, Metabolic and Biomolecular Engineering National Research Laboratory, Korea Advanced Institute of Science and Technology, Daejeon, South Korea*
- SANG YUP LEE • *Metabolic and Biomolecular Engineering National Research Laboratory, Department of Chemical and Biomolecular Engineering, Department of Biosystems, Bioinformatics Research Center, BioProcess Engineering Research Center and Center for Ultramicrochemical Process Systems, Korea Advanced Institute of Science and Technology, Daejeon, South Korea*

- SEOJU LEE • *Neose Technologies Inc., Horsham, PA*
- YAN-HUI LIU • *Schering-Plough Research Institute, Union, NJ*
- SI LUSHENG • *Institute for Cancer Research, College of Life Science and Technology, Xi'an Jiaotong University, Xi'an, Peoples Republic of China*
- STACEY MA • *Department of Analytical Chemistry, Genentech Inc., South San Francisco, CA*
- YUH-FUN MAA • *ALZA Corporation, Mountain View, CA*
- GARGI MAHESHWARI • *Merck & Co., Inc., Rahway, NJ*
- FABIO MALAVASI • *Laboratory of Immunogenetics, Department of Genetics, Biology and Biochemistry, University of Torino Medical School, Turin, Italy and Research Center for Experimental Medicine (CeRMS), San Giovanni Battista Hospital, Turin, Italy*
- ROSALYN J. MARCHANT • *Department of Biosciences, University of Kent, Canterbury, Kent, UK*
- JOSEPH E. MCCLELLAN • *Department of Characterization and Analytical Development, Wyeth BioPharma, Andover MA*
- TERESA R. MCCURDY • *Research and Development Department, Canadian Blood Services, Hamilton, Ontario, Canada*
- AARON P. MILES • *Biochemical Assay Development and Quality Control, Malaria Vaccine Development Branch, National Institute of Allergy and Infectious Diseases, Rockville, MD*
- CHARLES E. MITCHELL • *Bioproduct Research and Development, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN*
- KATHY MOORHOUSE • *Department of Quality Control Clinical Development, Genentech Inc., South San Francisco, CA*
- TERUHISA NAKASHIMA • *Blood Products Research Department, The Chemo-Sero-Therapeutic Research Institute, Kumamoto, Japan*
- WASSIM NASHABEH • *Department of Quality Control Clinical Development, Genentech Inc., South San Francisco, CA*
- KENNETH J. O'CALLAGHAN • *Department of Biosciences, University of Kent, Canterbury, Kent, UK*
- YEMI ONAKUNLE • *Lonza Biologics plc, Slough, UK*
- AMULYA K. PANDA • *Product Development Cell, National Institute of Immunology, New Delhi, India*
- HIMAKSHI K. PATEL • *Department of Characterization and Analytical Development, Wyeth BioPharma, Andover MA*
- BERNARDO PEREZ-RAMIREZ • *Scientific Director, BioFormulations Development, Genzyme, Framingham, MA*
- ANDREW G. POPPLEWELL • *Celltech R&D, Slough, UK*
- THOMAS J. PORTER • *Department of Characterization and Analytical Development, Wyeth BioPharma, Andover MA*
- ALICE RIGGIN • *Bioproduct Research and Development, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN*

- SCOTT ROSENTHAL • *Bayer Corporation Biological Products, Clayton, NC*
- JASON C. ROUSE • *Department of Characterization and Analytical Development, Wyeth BioPharma, Andover MA*
- ALLAN SAUL • *Malaria Vaccine Development Branch, National Institute of Allergy and Infectious Diseases, Rockville MD*
- MUKESH SEHDEV • *Celltech R&D, Slough, UK*
- SCOTT P. SELLERS • *ALZA Corporation, Mountain View, CA*
- WILLIAM P. SHEFFIELD • *Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada*
- SURINDER M. SINGH • *Product Development Cell, National Institute of Immunology, New Delhi, India*
- C. MARK SMALES • *Protein Science Group, Department of Biosciences, University of Kent, Canterbury, Kent, UK*
- MARIANGELA SPITALI • *Celltech R&D, Slough, UK*
- JOHN J. STECKERT • *Characterization & Analytical Development, Wyeth BioPharma, Andover, MA*
- BHASKAR THYAGARAJAN • *Poetic Genetics, LLC, Burlingame, CA*
- KAZUHIKO TOMOKIYO • *Blood Products Research Department, The Chemo-Sero-Therapeutic Research Institute, Kumamoto, Japan*
- MICK F. TUIE • *Department of Biosciences, University of Kent, Canterbury, Kent, UK*
- MICHÈLE F. UNDERHILL • *Department of Biosciences, University of Kent, Canterbury, Kent, UK*
- MARTEN VEENHUIS • *Eukaryotic Microbiology, Groningen Biomolecular Sciences and Biotechnology Institute (GBB), University of Groningen, Haren, The Netherlands*
- MARCIO VOLOCH • *Transkaryotic Therapies Inc., Cambridge, MA*
- A. NEIL C. WEIR • *Celltech R&D, Slough, UK*
- FLORIAN M. WURM • *Laboratory of Cellular Biotechnology, SV-IGBB-LBTC, EPFL, Lausanne, Switzerland*
- DAVID C. WYLIE • *Biotechnology Development, Schering-Plough Research Institute, Union, NJ*
- LEI XIE • *Schering Plough Research Institute, Union, NJ*
- WANG YILI • *Institute for Cancer Research, College of Life Science and Technology, Xi'an Jiaotong University, Xi'an, Peoples Republic of China*
- LEI YU • *Bioproduct Research and Development, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN*
- DAMING ZHU • *Biochemical Assay Development and Quality Control, Malaria Vaccine Development Branch, National Institute of Allergy and Infectious Diseases, Rockville, MD*