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Therapeutic Proteins

Methods and Protocols

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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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