
Preface

The huge potential for gene therapy to cure a wide range of diseases has led to high expectations and a great increase in research efforts in this area. The first human gene therapy protocol was conducted in 1990 by W. French Anderson and showed promising results. Over the following years, more than 1,500 gene therapy protocols were approved for clinical trials, illustrating the rapid growth of this field. Furthermore, with the sequencing of the human genome and the development of advanced technologies for the identification of genes and their function, the number of candidate diseases for gene therapy has continued to increase. However, the efficient transfer of a therapeutic gene into human cells depends upon the technology used for gene therapy. A number of delivery systems are in use, which either involve physical delivery of naked DNA or the use of viral vectors. The protocols of the latter system are the subject of this book.

There is a large and rapidly growing body of literature on methods for gene delivery involving the use of viral vectors. This is because genes are delivered more efficiently by viral vectors, compared to DNA transfection. Vectors derived from retroviruses and adenoviruses are used in the majority of gene therapy clinical trials to date. However, vectors derived from adeno-associated viruses, poxviruses, herpes simplex viruses, and baculoviruses are receiving increasingly more attention in the field of gene therapy. The properties of each of these vectors are described in Chapter 1, while Chapter 2 gives answers based on examples of clinical trials to the question of why gene therapy has not yet become an effective treatment for genetic disease.

Methods in Molecular Biology: Viral Vectors for Gene Therapy brings together the knowledge and experience of those who are employing methodology of virus production, transferring protocols, and evaluating the efficacy of gene product. This is a comprehensive methods book that provides basic principles for the development of gene therapy viral products that are safe and effective. Chapters presenting protocols in readily reproducible, step-by-step fashion, opening with an introductory overview, a list of the materials and reagents needed to complete the experiment, and followed by a detailed procedure that is supported with a helpful notes section offering tips and tricks of the trade as well as troubleshooting advice. There are chapters on production, purification, and characterization of the most popular viral vector systems of adenovirus, retrovirus, and adeno-associated virus (Chapters 5–11). The methodologies are in most cases simple, tested, and robust processes. The protocols for the less common viral vector systems of baculovirus, herpes virus, and measles virus are presented in Chapters 12–14. The growing interest in these vectors has created a strong demand for large-scale manufacturing and purification procedures.

In view of the interest of many laboratories and practitioners in the preclinical and clinical application of gene therapy vectors, it seems appropriate to include chapters to describe protocols on the *in vivo* gene delivery into CD34 and mesenchymal cells as non-exhaustive examples for *in vivo* gene transfer (Chapters 15 and 16). In this context, we have also included Chapter 11 on characterization and quality control testing of *in vivo* gene delivery of AAV viral vectors for the treatment of muscular and eye diseases to present an example on a subject which is still today very much en vogue for most scientists.

Chapter 3 presents basic considerations concerning the characterization of cell banks for the production of viral vectors. It describes the advantages and disadvantages of the most widely used cell lines, HEK293. The importance of viral purification in manufacturing is now widely recognized, and information is presented here (Chapter 4) on the most commonly used purification methods and chromatographic options available for large-scale processes.

Gene therapy raises many unique ethical concerns. Although germ line gene therapy is controversial, somatic gene therapy is morally acceptable for treating diseases since all effects of therapy end with the life of the patient, at the very latest. Chapter 17 explores some of the ethical issues surrounding human gene therapy. The final chapter (Chapter 18) presents examples of clinical trials and examines the processes of good clinical practice, good manufacturing practice, and regulations for conducting gene therapy trials.

Protocols in gene therapy are not well understood by many scientists who will find this book to be of interest. The material is addressed primarily to those interested in viral gene therapy, but topics will also be of interest to scientists in virology, biomedicine, molecular biology, cell culture, preclinical and clinical trials, cell banking, manufacturing, quality control as well as medical practitioners. It will provide an invaluable resource for students and researchers involved in the development of expression systems, gene delivery systems, and therapeutic products. The editors come from industrial gene therapy (O.-W. Merten) and academic bioprocessing (M. Al-Rubeai) backgrounds and are therefore well placed to ensure that the contents are addressed to and understandable by a wide range of readers. We are enthusiastic for the cause of gene therapy – we hope that our readers find inspiration to explore further its potential themselves and that this work helps their rapid progress.

Finally, we thank all the contributors, the series editor John Walker, and Humana Press for their efforts which made this volume possible.

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