
Preface

The past decade has witnessed a spectacular explosion in both the development and use of transgenic technologies. Not only have these been used to aid our fundamental understanding of biologic mechanisms, but they have also facilitated the development of a range of disease models that are now truly beginning to impact upon our approach to human disease. Some of the most exciting model systems relate to neurodegenerative disease and cancer, where the availability of appropriate models is at last allowing radically new therapies to be developed and tested. This latter point is of particular significance given the current concerns of the wider public over both the use of animal models and the merits of using genetically modified organisms.

Arguably, advances of the greatest significance have been made using mammalian systems—driven by the advent of embryonic stem-cell-based strategies and, more recently, by cloning through nuclear transfer. For this reason, this new edition of *Transgenesis Techniques* focuses much more heavily on manipulation of the mammalian genome, both in the general discussions and in the provision of specific protocols.

Of all mammalian experimental systems, the laboratory mouse is probably the most widely used, a situation that almost certainly derives from the fact that it is genetically the most tractable. This second edition, therefore, devotes much space to methodologies required for the creation and maintenance of genetically modified murine strains. In addition to protocols for conventional pronuclear injection, chapters have been included covering alternative routes to the germline, by either retroviral or adenoviral infection. Extensive coverage is also given to the generation, maintenance, and manipulation of embryonic stem cell lineages, since this is now widely recognized as an indispensable approach to genotype–phenotype analysis. Part V contains protocols to facilitate gene targeting and so permit both constitutive and conditional gene targeting. The latter approach, reliant on either the Cre-lox or the Flp-frt system, is rapidly gaining favor as a method of choice for the analysis of null mutations because it solves the twin difficulties of embryonic lethality and developmental compensation—two problems that have hampered the analysis of simple “knock-out strains.”

The proliferation of newly engineered murine strains has given rise to one problem within the field, namely, that of the long-term storage of lines for which

there might be no immediate requirement. Within many laboratories, this is now far from a trivial problem, and, therefore, methodologies are included that detail the cryopreservation of both male and female germ lines.

Although the mouse is currently the most genetically tractable system, it is not without its limitations and clearly cannot deliver all appropriate experimental or commercial systems. Transgenic manipulation of the rat germline is now delivering valuable models across a range of fields, perhaps most notably in neurobiology and in the study of vascular diseases. This edition, therefore, also focuses on the generation, maintenance, and cryopreservation of rat transgenic lines.

The mouse and the rat remain essentially laboratory models. However, perhaps the most radical change to occur within the field relates to our emerging ability to genetically engineer livestock. In particular, the advent of cloning as a viable technology has wide ramifications for the scientific and industrial communities as well as for the wider public. Protocols are given for the generation of transgenic sheep by nuclear transfer, and, furthermore, the potential implications and future directions of large animal transgenesis are discussed in some detail.

Finally, this second edition carries a very detailed part relating to the basic analysis of transgenic organisms. Although many of the techniques included are widely used throughout molecular biology, those pertinent to transgenic analysis have been brought together to facilitate the rapid analysis of phenotype. Used in conjunction with the plethora of techniques relating to the generation and maintenance of transgenic strains, the contributors and I anticipate that this new edition of *Transgenic Techniques* will prove an invaluable asset to any laboratory either already engaged in transgenic manipulation or setting out along this route.

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