
Preface

Simian virus 40 gained notoriety in the 1960s because it was found to be a contaminant of polio and adenovirus vaccines that had been administered to millions of healthy individuals worldwide. The public health implications of this revelation provided the initial impetus for an in-depth study of SV40 biology. Later work showed that SV40 DNA sequences as well as infectious virus are in fact found in human tumors and may have contributed to oncogenesis. It also turned out that SV40 uses mostly cellular machinery to carry out many steps in viral infection, which makes it a powerful probe for examining many fundamental questions in eukaryotic molecular biology. *SV40 Protocols* consolidates a number of well-tested step-by-step techniques in one volume; experts with hands-on experience in particular methods give detailed accounts of their optimized experimental protocols, so that the beginner, as well as more experienced researchers, may readily overcome problems of ambiguity often present in the literature.

As with other DNA tumor viruses, the response of cultured cells to SV40 infection depends upon the species being infected. Monkey cells support virus production, which leads to their death, whereas rodent cells produce only the early proteins and acquire a transformed phenotype. Thus, *SV40 Protocols* is organized in two sections. The first relates to assays of the lytic cycle of the virus, and the second deals with transformation. The first section starts with a chapter on the basic techniques for growth of SV40 and its mutants in tissue culture, which would be valuable for the beginner. Three chapters follow on techniques for the growth and detection of two SV40-related human viruses, BKV and JCV, which would be of particular interest to those involved in clinical research.

Complicated biochemical processes cannot change radically once solved by evolution. Since SV40 DNA replication is carried out mostly by the cellular machinery, insights gained into its replication are likely to be relevant to eukaryotic DNA replication in general. Similarly, the study of SV40 transcription and its regulation has provided valuable clues to the mechanisms of eukaryotic transcription. Therefore, the next three chapters constitute detailed accounts of protocols for SV40 DNA replication and transcription, both in vivo and in vitro.

The field of gene therapy has evolved from an investigative curiosity to a major focus of medical research. Therefore, the next two chapters of this section are on the use of SV40 virus, or SV40 pseudovirions made in insect cells, as vectors for human gene therapy. The section ends with a chapter on the use of retroviral vectors for the expression of SV40 tumor antigens in cultured cells, an approach that is useful in gene expression in general and prepares the reader for the next section dealing with SV40-mediated neoplastic transformation.

Work on SV40 neoplasia has yielded a plethora of information on cell growth controls and led to the discovery of two families of antioncogenes, p53 and the retinoblastoma susceptibility gene products. This section starts with a detailed account of biological assays of neoplastic transformation that are applicable to any system. The next two chapters describe methods to assess the effects of SV40 large T antigen (SVLT) expression upon adipocytic differentiation and upon establishment of cells in culture. Three chapters follow, each dealing with proteins associated with and affected by SVLT: p53, Rb, and Ras. Chapters on the effects of the second SV40 tumor antigen, small T, cytotoxic T lymphocytes in SV40 infections, and the detection of SV40 sequences in human tissues follow. The section ends with a chapter on the use of SVLT transgenic animals as models for the study of multistage tumor development.

All chapters in *SV40 Protocols* offer thorough technical accounts of the methods treated and include discussions of the problems and pitfalls that may be encountered as well as valuable troubleshooting advice. An Appendix at the end of the volume lists all companies whose products are cited in the text. Since a company may stop manufacturing a given reagent, whereas others may start later, an Internet directory address is also provided. Note that the performance of many reagents may vary from lot to lot and many reagents may come in kits. In these cases, the precise recommendations of the manufacturer for use of a particular reagent must take precedence over the conditions described.

First and foremost I would like to thank all of the contributors: their high-quality submissions and valuable suggestions made this volume possible. Special thanks go to Ximena Montano for her many recommendations of potential contributors. I also thank the series Editor, John Walker, for his valuable advice, especially, at the initial stages.

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