

---

## Preface

Parkinson's disease is a progressive neurodegenerative disorder characterized clinically by tremor, rigidity, slow movements, and postural instability. Pathologically, dopaminergic neurons of the substantia nigra bear the brunt of the degeneration, though other neuronal groups can be affected as well. Although Parkinson's disease is the only neurodegenerative disorder for which effective therapies are available, these treatment options are only symptomatic, do not influence the underlying degenerative process, and are associated with a high incidence of complications, particularly with their long-term use. The progressive nature of the disease and the limitations of its palliative therapies result in significant functional impairment. The chronic disability and the increased prevalence of the disease with the prolongation of life expectancy in developed countries make the social and economic impact of this disease quite high. Fortunately, systematic basic and clinical research in this disease has yielded major new advances that render patients' hopes for a cure considerably closer to reality.

The application of molecular biologic methodologies in the study of Parkinson's disease has begun to have a major impact only in recent years. Consequently, the utility of these technologies is largely in the research arena, although their clinical applications are now being realized. Therefore, the goal of *Parkinson's Disease: Methods and Protocols* is to introduce scientists and clinicians interested in Parkinson's disease, in particular, and neurodegenerative diseases, in general, to the progress and potential of molecular biology and genetics in unraveling the mysteries of these disorders and in devising innovative therapeutic strategies. The timeliness of this subject stems from the recent explosion of information about the genetic etiologies of Parkinson's disease. Naturally, these findings have sparked tremendous research interest and multiplied opportunities to elucidate the molecular pathogenesis of this disease. In addition, advances in cellular and molecular biology have fueled the need to develop new and improved therapeutic modalities for this disorder.

Genetic discoveries in pedigrees with familial Parkinson's disease have revolutionized our concept of this disorder. These findings have now made it clear that Parkinson's disease is not a single disorder. Rather it represents multiple underlying defects with similar clinical phenotypes. This etiologic disparity, in fact, demands the pursuit of many different research hypotheses about the molecular pathogenesis of the disease and requires the use of varied experimental tools.

In short, these genetic discoveries constitute the ground work for the next set of important questions in this field, namely, how these genetic defects result in the death of dopaminergic neurons and how to prevent or slow this process.

*Parkinson's Disease: Methods and Protocols* covers the main basic research disciplines and molecular methodologies that are actively being pursued in studies of Parkinson's disease. It compiles state-of-the-art molecular methods that are currently being used to advance our understanding of the etiologies and pathogenesis of the neurodegeneration in this disorder. This book also provides a concise and comprehensive review of the background and significance of each protocol described in order to give the reader a fundamental understanding of the subject matter and its implications.

Four broad fields relevant to Parkinson's disease are covered in this book. Part I, Genetics, describes the two established gene defects known to cause this disease, namely, missense mutations in the  $\alpha$ -synuclein gene, which result in autosomal dominant disease, and deletions or point mutations in the parkin gene, which lead to autosomal recessive disease. Part II, Molecular Pathogenetic Studies, describes several recent biochemical hypotheses and findings thought to be important in the death of nigral dopaminergic neurons. These include experiments to elucidate biochemical and structural changes that result from  $\alpha$ -synuclein mutations, characterization of apoptotic dopaminergic neurons, and investigating the role of nitric oxide and oxidative stress in the death of these neurons. Part III, Molecular Aspects of Basal Ganglia Function, describes methods used to study various aspects of the nigrostriatal neural circuitry, including quantification of tyrosine hydroxylase mRNA, immunochemical studies of dopamine transporters, transcription control mechanisms for dopamine receptor genes, in situ hybridization for genes expressed in the basal ganglia, and the functional regulation of NMDA receptors in striatal medium spiny neurons in experimental parkinsonism. Lastly, Part IV, Molecular Therapies, describes novel experimental treatment approaches that have been tested recently in animal models of Parkinson's disease, including intracerebral delivery of trophic factors, grafting genetically engineered cells into the striatum using either naked cells or encapsulated implants, and the use of neural stem cells.

We hope that *Parkinson's Disease: Methods and Protocols* will enhance the awareness of the scientific and medical communities about recent landmark discoveries in Parkinson's disease. This book makes currently employed research protocols readily available under one cover for scientists who plan to enter this field. We trust this will attract new investigators to study Parkinson's disease and, therefore, accelerate the progress toward a cure.

**M. Maral Mouradian, MD**



<http://www.springer.com/978-0-89603-761-8>

Parkinson's Disease

Methods and Protocols

Mouradian, M.M. (Ed.)

2001, XI, 317 p., Hardcover

ISBN: 978-0-89603-761-8

A product of Humana Press