

Preface

PARKINSON'S DISEASE (PD) WAS ONCE A TABOO SUBJECT, with affected individuals making every effort to conceal the physical manifestations of their movement disorder. This is no longer the case. Today, rather than hiding their condition, politicians, artists, and world leaders with PD openly acknowledge their diagnosis and share how they cope with its medical, social, and emotional challenges.

However, while public awareness of PD is now widespread, our understanding of why and how the disease develops and progresses still lags behind. For every question answered, clinical and basic researchers in the field uncover many more unanswered ones. If we are to develop effective therapies for this debilitating disorder, we must first unravel the pathobiology of PD. Achieving this will require bringing together talented individuals with diverse skill sets and perspectives to work collaboratively across disciplines. Clinicians should be encouraged to engage with the basic physiology, molecular mechanisms, and cellular biology of PD, while basic researchers must gain exposure to the finer clinical aspects of the disease and develop an understanding of the day-to-day realities faced by affected individuals.

We often hear from colleagues—both clinicians and basic scientists—who want to contribute to PD research but struggle to find accessible resources. Clinicians frequently find basic science texts filled with technical jargon and abstract concepts, while basic scientists find clinical textbooks too cryptic or detailed for nonspecialists. This gap in resources led us to wonder: Is there a single book we could recommend to both groups? A book that bridges the clinical and basic science aspects of PD under one cover—one that provides a broad yet insightful overview rather than an exhaustive compendium of every detail? Such a book would serve as a didactic tool, offering fundamental knowledge alongside key takeaways and practical insights.

With this vision in mind, Cold Spring Harbor Laboratory Press partnered with us in 2012 to publish the first edition of this monograph, aimed at providing a comprehensive bench-to-bedside understanding of PD. Encouraged by its reception, we were recently invited to produce this second edition, which includes both updated chapters reflecting advancements since 2012 and new chapters on critical topics such as disease progression, cell-based replacement therapies, biomarkers, lipid dysregulation, and the gut–brain axis. These subjects were either absent from the first edition or have since emerged as essential areas of study. Each expert contributor was asked to write their chapter as if guiding a new student or faculty member—whether clinician or basic scientist—who is eager to enter the field.

Readers will begin their journey with Goetz's chapter on the history of PD, setting the stage for understanding how this neurological disorder was initially identified and defined. From there, Patel et al., Irmady and Przedborski, along with Dickson, provide the clinical foundations, disease progression insights, and neuropathological underpinnings of PD. Among other key points, they highlight that PD's clinical features are not exclusive to the disease but are shared by a number of other conditions. They also emphasize that while PD is primarily known for its motor symptoms and the loss of dopaminergic neurons, it also involves nonmotor symptoms and degeneration of non-dopaminergic neurons, all of which play a crucial role in disease expression and disability.

As with other prominent adult-onset neurodegenerative diseases such as Alzheimer's and amyotrophic lateral sclerosis, PD is primarily sporadic. However, in a small subset of cases, PD follows a familial pattern, inherited as a dominant or recessive trait linked to various gene mutations. These rare genetic forms of PD are under intense study, as understanding the normal functions of these genes and how mutations disrupt them may provide critical insights into the pathobiology of sporadic PD.

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Several chapters explore the genetics of PD, beginning with an introduction by Westenberger et al., followed by discussions on specific genes and their products, including α -synuclein (Vekrellis et al.) and LRRK2 (Pfeffer and Alessi). The section concludes with a key discussion by Menon on genomics, offering a broader perspective that considers all genes and their interactions to provide insights into complex diseases such as PD.

Beyond genetics, PD research also seeks to understand how neurodegeneration alters the functional neuroanatomy of the basal ganglia, leading to the motor abnormalities observed in patients. To explore this, Lanciego and Obeso, Wichmann, and Nakano et al. examine the disease through the lenses of functional neuroanatomy and brain imaging, highlighting how therapeutic strategies that modulate specific neural pathways provide symptomatic relief for PD patients. The section concludes with a discussion and an addendum by Kayhanian and Barker on dopamine cell-based replacement therapies, which, like neuromodulation, aim to provide symptomatic benefit. Lastly, Lodge and Agin-Liebes contribute a chapter on biomarkers, exploring their potential role in early diagnosis, disease monitoring, and the development of targeted therapies.

Because experimental models are essential to studying the neurobiology of PD, a series of chapters by Bezard et al., Tieu et al., and Dawson and Dawson cover the topic, ranging from primate to rodent models and from toxin-based to genetic-based models.

The final section of the book explores emerging and significant pathogenic mechanisms in Parkinson's disease. Chapters by Schon et al., Area-Gómez et al., Martinez-Vicente and Vila, Gao et al., Elyaman, and Oludipe et al. examine key topics, including the roles of mitochondria, lipids, autophagy and protein quality control, the gut-brain axis, and the innate and adaptive immune systems in the disease process.

This is the roadmap of the book. Before we begin, we invite you to embark on this journey from bench to bedside with curiosity and enthusiasm. We hope you find as much value in reading this volume as our distinguished colleagues and we did in preparing it.

Finally, we extend our gratitude to the authors who contributed their time and expertise, and to Danett Gil, Barbara Acosta, and Richard Sever at Cold Spring Harbor Laboratory Press, whose invaluable assistance and guidance made this book possible.

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