METHODS IN MOLECULAR BIOLOGY™

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Dopamine

Methods and Protocols

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Cover illustration: The image depicts a whole mount adult *Drosophila* brain triple-labeled with rabbit anti-GFP antibody (green), mouse anti-FasII (1D4) antibody (red) and DAPI (blue) which mark the dopaminergic neurons (revealed by genetically labeling with *ple-GAL4,UAS-mCD8::GFP*), axon tracts of the mushroom bodies and the central complex, and all brain cell nuclei, respectively. Note in the merged image the projections of dopamine neurons to areas of the mushroom body, the *Drosophila* center for learning and memory, and to the central complex, which contributes to the regulation of locomotion. (See Chapter 13.)

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Preface

Dopamine, a catecholamine transmitter, plays a number of important physiological roles in the brain and body. Clues to dopamine's role in motivation and learning have come from over 50 years of studies in laboratory animals, which have included rodents and nonhuman primates. In more recent years, studies on the role of dopamine in disease have opened new avenues of research and discovery. Genetic cloning has further enabled studies of dopamine in other species such as *Drosophila melanogaster* and *Danio rerio*. This edition of *Methods in Molecular Biology* brings together and provides detailed protocols on leading approaches in the study of dopamine within biological systems.

In the brain, dopamine functions as a key neurotransmitter in regions such as the cortex and striatum. Dopamine is also an important modulator of ion balance in the kidney and adaptation to light in the retina. The many effects of dopamine on physiological systems and organs are dependent on a class of receptors, which are coupled to heterotrimeric G proteins. In mammals, five dopamine receptors (D1–D5) have been identified. A fundamental aspect of dopamine function is the localization of these receptors at the membrane, their interaction with signaling and regulatory molecules, and their ability to assemble into higher-order receptor oligomers (with dopamine and non-dopamine receptors) within cells.

In many species, dopamine plays a major role in reward-driven learning. Indeed, almost every type of reward that has been studied increases dopamine transmission in the brain, and a variety of highly addictive drugs, including stimulants such as cocaine and methamphetamine, act directly on the dopamine system. Several prominent diseases of the nervous system are associated with dopamine. In particular, alterations in dopamine levels are intimately linked with the onset and progression of Parkinson's disease, which results from the death of dopaminergic neurons within the substantia nigra. Schizophrenia, a disease of multiple genes and origins, has long been linked to dopamine imbalances within the striatum and cortex with the majority of classical antipsychotic drugs acting as antagonists at D2 receptors and many newer generation antipsychotics maintaining an effect on D4 receptors.

This book is of interest to a range of scientists including cellular and molecular biologists, electrophysiologists, and pharmacologists. The chapters are intended for students and experts alike and for anyone interested in exploring the vast field of dopamine research. The book is divided into four parts based on methods: cellular/biochemical, imaging, genetics, and electrophysiology. Presented are chapters with step-by-step, clear, and precise instructions for various research procedures. This includes protocols for bioluminescence and fluorescence imaging, receptor immunoprecipitation and proteomic analysis, creation and characterization of a mouse model of Parkinson's disease, real-time measurement of dopamine in the brain, and modeling signal transduction in silico.

This volume is the product of contributions from experts and key figures within the field. I would like to thank the authors for their outstanding work and cooperation during the preparation of the volume. Specifically, I would like to thank the series editor, Professor John Walker, for his support during the assembly of this book.

Nadine Kabbani, Ph.D.

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