PREFACE

This issue of *Progress in Molecular Biology and Translational Science* is focused on neuroepigenetics, a still relatively "young" area of research exploring the roles of chromatin structure and function in the context of development, adulthood, and disease. In the broadest sense, epigenetics could be viewed as the mechanisms and molecular bridges by which countless internal and external factors (re)organize the genomic material that is packaged inside the nuclei of brain cells, thereby potentially affecting synaptic plasticity and behavior. Epigenetic mechanisms, which among many others include proper regulation of DNA cytosine methylation, histone modifications, and nucleosomal organization (a nucleosome is the elementary unit of chromatin, with 147 bp of genomic DNA wrapped around a core of eight histone proteins), are thought to play an important role in various neurodevelopmental and neurological disorders.

Some of these key concepts linking epigenetic mechanisms to neuronal plasticity and (mal)adaptive mechanisms in the immature and also adult brain are highlighted in the eight chapters published in this issue. The first chapter, written by Jarome, Thomas, and Lubin, provides a general overview and detailed discussion on regulatory mechanisms governing covalent DNA and nucleosomal histone modifications during memory formation and storage in the mammalian brain. Next in Chapter 2, Rampp, Binder, and Provençal discuss gene × environment interactions in the context of traumatic memory and posttraumatic stress disorder, with particular focus on steroid hormone and other stress-responsive pathways. In Chapter 3, Hitchcock and Lattal describe the increasingly recognized importance of histone methylation and acetylation and other modifications for plasticity-dependent phenomena in the brain's reward circuit, and the potential implications for the treatment of addiction and substance abuse and dependence. Chapters 4, written by Guidotti, Dong, Tueting, and Grayson, and 5, written by Lolak, Suwannarat, and Lipsky, discuss epigenetic risk factors in the context of mood and psychosis spectrum disorders, including schizophrenia and depression. Next, Lopez-Atalaya, Valor, and Barco in Chapter 6 provide a highly informative discussion of Rubinstein–Taybi syndrome (RSTS), a neurodevelopmental syndrome caused by mutations in the genes encoding the lysine acetyltransferases CBP and p300. RSTS serves as a prototype example of monogenic neurological disease associated

with epigenetic dysregulation (histone acetylation in this case), affecting both the developing brain and mature circuitry via multiple mechanisms. While aforementioned reviews focus on environmental or genetic mechanisms directly impacting the epigenome of brain cells, Chapter 7 by Galler and Galler Rabinowitz explores intergenerational effects of early adversity, including the potential role of epigenetics in intergenerational transmission. The final chapter of this issue, written by Mitchell, Roussos, Peter, Tsankova, and Akbarian, embarks on future developments in the field of neuroepigenetics (which will include the exploration of the nonrandomness in three-dimensional chromosomal organization and other principles often referred to as "higher order chromatin") and how such type of molecular approaches could provide further insights into genetic and epigenetic risk architecture of cognitive disorders unique to the human brain.

We, as volume editors, have asked the authors of these various chapters not only to summarize the evidence collected so far in their field but also to highlight some of the important topics that are subject to ongoing debate or hitherto underexplored. It is our hope and expectation that such type of discussion will further stimulate interest in epigenetic approaches and excite the younger generation of neuroscientists about these lines of research. Just to mention a few examples of debate mentioned in this issue: Chapter 1 highlights the bulk of the epigenetics literature pertaining to the learning and memory field and is preoccupied with mechanisms that are primarily relevant for initial acquisition of memory, while much less attention has been given to the equally important stages of consolidation, retrieval, and extinction. This chapter also highlights the potential epigenetic targets that may serve to improve or enhance memory function, while Chapter 5 cautions on the effects of neurological therapies on these epigenetic mechanisms. Several chapters include some remarks on tissue specificity of epigenetic signals, which is particularly relevant in the context of approaches aimed at exploring epigenetic signals in blood and the periphery as biomarkers for brain-related disease (Chapter 2) or chromatin state mappings in brain tissue with its extremely complex and highly heterogenous mixture of neuronal and glial subpopulations (Chapter 8). Furthermore, Chapter 3 points to two other important problems in neuroepigenetics including the often unresolved question of correlational association versus causal mechanism, and the difficulties and challenges in linking the molecular and behavioral phenotypes to the prevailing theories on reward and memory. Chapter 7 touches upon the still very novel and provocative concept of transgenerational inheritance.

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SCHAHRAM AKBARIAN
FARAH LUBIN