

The Role of Epigenetic Mechanisms in the Regulation of Gene Expression in the Nervous System

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Neuroepigenetics is a newly emerging field in neurobiology that addresses the epigenetic mechanism of gene expression regulation in various postmitotic neurons, both over time and in response to environmental stimuli. In addition to its fundamental contribution to our understanding of basic neuronal physiology, alterations in these neuroepigenetic mechanisms have been recently linked to numerous neurodevelopmental, psychiatric, and neurodegenerative disorders. This article provides a selective review of the role of DNA and histone modifications in neuronal signal-induced gene expression regulation, plasticity, and survival and how targeting these mechanisms could advance the development of future therapies. In addition, we discuss a recent discovery on how double-strand breaks of genomic DNA mediate the rapid induction of activity-dependent gene expression in neurons.

Key words: DNA double strand breaks; DNA methylation; MeCP2; polycomb repressive complex; topoisomerase II

Introduction

Organs, including the brain, are determined by the pattern of gene expression that emerges in each cell lineage during development. The key drivers of these genetic programs are proteins that recognize specific combinations of nucleotides that specify a genomic address. By binding to their sites, either alone or in conjunction with others, these sequence-specific DNA binding proteins or “transcription factors” determine which genes are actively expressed and which must remain silent. Several lines of evidence suggest, however, that there are more constraints on development and differentiation than simply the availability of transcription factors. For example, although cells of the liver, skin, intestine, etc., possess the entire genome, it took many years to find ways of converting a differentiated cell into a stem cell that could once again give rise to the whole organism. Even now, reversal of differentiation is still a highly inefficient process. A likely reason is that “epigenetic marking” of the genome, laid down during the developmental history of the cell, “conditions” the genome’s response to transcription factors and is therefore an

essential additional factor in determining programs of gene expression. “Epigenetics” refers to the study of ways in which chromosome regions adapt structurally so as to register, signal, or perpetuate local activity states (Bird, 2007).

A key feature of epigenetic marking is that it is stable, sometimes across cell generations, but also reversible. It is mediated by proteins that add, remove, or interpret the modified structures, referred to as “writers,” “erasers,” and “readers” respectively. Epigenetic systems include DNA methylation (Bird, 2002), and the polycomb/trithorax system (Francis and Kingston, 2001). Other epigenetic mechanisms involve RNA (Vaishij et al., 2002; Volpe et al., 2002) or the silencing or activation of genes due to their localization within the nucleus (Brown et al., 1997; Mahy et al., 2002). These and other processes appear to be closely interwoven with histone modification, which is itself a diverse, complex system of chromosome marking (Jenuwein and Allis, 2001). Histone proteins stably associate with DNA to form a repeating structural unit that organizes the genome. The combination of DNA and periodic histone complexes is referred to as chromatin, resembling beads on a string of DNA. In addition to their structural role, histones possess exposed tails that can be marked by chemical modification. For example, acetylation of histone tails by histone acetyltransferases loosens the contact with DNA and also creates binding sites for protein readers that facilitate gene expression. Acetylation is removed by histone deacetylase-containing complexes, which therefore inhibit the activity of genes. Methylation of histone tails can be either activating or repressive, depending on the precise amino acid that is affected. For example, the function of the Polycomb Repressive Complex 2 (PRC2) is mediated by its enzymatic components Ezh1 and Ezh2, which catalyze methylation of lysine 27 on histone H3 leading to gene silencing (Müller et al., 2002). There is evidence that PRC2 is essential in developing neu-

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Regulation Of Gene Expression In The Nervous System

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Regulation Of Gene Expression In The Nervous System:

Regulation of Gene Expression in the Nervous System Anna Maria Giuffrida Stella, Jean de Vellis, J. Regino Perez-Polo, 1990-07-19 Offers an up to date account of the latest research findings concerned with the regulatory mechanisms of gene expression in neuronal and glial cells under different conditions The book explores the cellular and neurobiological aspects of important phenomena of the nervous system and its role in health disease and injury Contributions from prominent scientists in the field address a variety of specific topics concerned with gene expression in the nervous system from growth hormonal and trophic factors to neural tissue reactions in injury or aging **Kaufman's Atlas of Mouse Development Supplement** Gillian Morriss-Kay, Shankar Srinivas, 2024-11-30 Kaufman's Atlas of Mouse Development Supplement Second Edition continues the stellar reputation of the original Atlas by providing updated in depth anatomical content and morphological views of organ systems The book explores the developmental origins of the organ systems following the original atlas as a continuation of the standard in the field for developmental biologists and researchers across biological and biomedical sciences studying mouse development In this new edition each chapter has been updated to include the latest research along with while new chapters on the functional aspects of mouse and human heart development the immune system and the inner ear These additions ensure an up to date resource for all biomedical scientists who use the mouse as a model species for understanding the normal and abnormal development of human systems Offers in depth anatomy and morphological views of organ systems and their developmental origins Includes the latest techniques for visualizing gene expression and other functional aspects of tissue and organ development Explores the links between mouse and human developmental processes Features high quality color images to help readers visualize key developmental processes and structures *Genetic Manipulation of the Nervous System*, 1995-11-24 Neuroscience Perspectives provides multidisciplinary reviews of topics in one of the most diverse and rapidly advancing fields in the life sciences Whether you are a new recruit to neuroscience or an established expert look to this series for one stop sources of the historical physiological pharmacological biochemical molecular biological and therapeutic aspects of chosen research areas The recent development of Gene Therapy procedures which allow specific genes to be delivered to human patients who lack functional copies of them is of major therapeutic importance In addition such gene delivery methods can be used in other organisms to define the function of particular genes These studies are of particular interest in the nervous system where there are many incurable diseases like Alzheimer's and Parkinson's diseases which may benefit from therapies of this kind Unfortunately gene delivery methods for use in the nervous system have lagged behind those in other systems due to the fact that the methods developed in other systems are often not applicable to cells like neurons which do not divide This book discusses a wide range of methods which have now been developed to overcome these problems and allow safe and efficient delivery of particular genes to the brain Methods discussed include virological methods physical methods such as

liposomes and the transplantation of genetically modified cells In a single volume therefore this book provides a complete view of these methods and indicates how they can be applied to the development of therapies for treating previously incurable neurological disorders

From Molecules to Networks Ruth Heidelberger, M. Neal Waxham, John H. Byrne, James L. Roberts, 2009-01-27 An understanding of the nervous system at virtually any level of analysis requires an understanding of its basic building block the neuron From Molecules to Networks provides the solid foundation of the morphologic biochemical and biophysical properties of nerve cells All chapters have been thoroughly revised for this second edition to reflect the significant advances of the past 5 years The new edition expands on the network aspects of cellular neurobiology by adding a new chapter Information Processing in Neural Networks and on the relation of cell biological processes to various neurological diseases The new concluding chapter illustrates how the great strides in understanding the biochemical and biophysical properties of nerve cells have led to fundamental insights into important aspects of neurodegenerative disease Written and edited by leading experts in the field the second edition completely and comprehensively updates all chapters of this unique textbook Discusses emerging new understanding of non classical molecules that affect neuronal signaling Full colour professional graphics throughout Includes two new chapters Information Processing in Neural Networks describes the principles of operation of neural networks and the key circuit motifs that are common to many networks in the nervous system Molecular and Cellular Mechanisms of Neurodegenerative Disease introduces the progress made in the last 20 years in elucidating the cellular and molecular mechanisms underlying brain disorders including Amyotrophic Lateral Sclerosis ALS Parkinson disease and Alzheimer s disease

Synapse Development and Maturation Pasko Rakic, John Rubenstein, Bin Chen, Kenneth Y. Kwan, 2020-05-29 Synapse Development and Maturation the latest release in the Comprehensive Developmental Neuroscience series presents the latest information on the genetic molecular and cellular mechanisms of neural development The book provides a much needed update that underscores the latest research in this rapidly evolving field with new section editors discussing the technological advances that are enabling the pursuit of new research on brain development This volume focuses on the synaptogenesis and developmental sequences in the maturation of intrinsic and synapse driven patterns Features leading experts in various subfields as section editors and article authors Presents articles that have been peer reviewed to ensure accuracy thoroughness and scholarship Includes coverage of mechanisms which regulate synapse formation and maintenance during development Covers neural activity from cell intrinsic maturation to early correlated patterns of activity

Gene Expression in the Central Nervous System Albert C. H. Yu, 1995 Gene expression is an active ongoing process that maintains a functional CNS as proteins are being made on a continual basis Processes such as learning and memory nerve cell repair and regeneration and its response to stress are critically dependent on gene expression This volume highlights the role of gene expression in normal CNS function and presents many research methods at the cutting edge of neuroscience

which will provide insight into therapeutic approaches through which the control of gene expression may be used in the treatment of many nervous system diseases *The Mouse Nervous System* Charles Watson, George Paxinos, Luis Puelles, 2011-09-22 *The Mouse Nervous System* provides a comprehensive account of the central nervous system of the mouse. The book is aimed at molecular biologists who need a book that introduces them to the anatomy of the mouse brain and spinal cord but also takes them into the relevant details of development and organization of the area they have chosen to study. *The Mouse Nervous System* offers a wealth of new information for experienced anatomists who work on mice. The book serves as a valuable resource for researchers and graduate students in neuroscience. Systematic consideration of the anatomy and connections of all regions of the brain and spinal cord by the authors of the most cited rodent brain atlases. A major section: 12 chapters on functional systems related to motor control, sensation and behavioral and emotional states. A detailed analysis of gene expression during development of the forebrain by Luis Puelles, the leading researcher in this area. Full coverage of the role of gene expression during development and the new field of genetic neuroanatomy using site specific recombinases. Examples of the use of mouse models in the study of neurological illness **Epigenetic Regulation in the Nervous System** J. David Sweatt, Michael J. Meaney, Eric J. Nestler, Schahram Akbarian, 2012-12-31 *Epigenetic Regulation in the Nervous System* addresses current understanding of the roles of epigenetic processes at the molecular cellular level, their impact on neural development and behavior, and the potential roles of these mechanisms in neurological and psychiatric disorders. This award winning volume spans molecular epigenetics, development, cellular physiology and biochemistry, synaptic and neural plasticity and behavioral models, and is unique in covering epigenetically based disorders of the central nervous system. Behavioral epigenetics is the study of how environmental factors alter behavior, addressing the fundamental mechanisms that shape development and individual vulnerability/resilience to adverse behavioral outcomes. By understanding the molecular mechanisms involved in epigenetic modulation, researchers may be able to develop targeted therapies for those individuals in whom it malfunctions. Edited by the most highly regarded leaders in the field, this book offers a comprehensive review of behavioral epigenetics and a balanced treatment of the strengths and weaknesses in experimentation in this area. Covering background material as well as topics of current interest, it serves both as a cutting edge resource and a foundational reference. The book will benefit neuroscience researchers and graduate students with an interest in the links between gene regulation and behavior, as will clinicians dealing with disorders such as addiction, depression, and schizophrenia. BMA Medical Book Awards 2014 Highly Commended Neurology. British Medical Association BMA Medical Book Awards 2014 First Prize Neurology. British Medical Association 2013 PROSE Award winner for Best in Reference Works and Best Single Volume Reference in Science from the Association of American Publishers. Presents a unified view of epigenetic mechanisms from behavior to genes and everything in between. Discusses clinically relevant disorders in the context of epigenetics research, making the volume appealing to clinicians as well as basic scientists. Provides

numerous practical examples for the new investigator to facilitate implementation of research in neuroepigenetics

Molecular Biology of the Cell, 2002 *Serotonin Receptors in Neurobiology* Amitabha Chattopadhyay, 2007-05-17 A number of developments spanning a multitude of techniques makes this an exciting time for research in serotonin receptors. A comprehensive review of the subject from a multidisciplinary perspective. *Serotonin Receptors in Neurobiology* is among the first books to include information on serotonin receptor knockout studies. With contributions from 1 **The Enteric Nervous System** John Barton Furness, Marcello Costa, 1987 **Untranslated Gene Regions and Other Non-coding Elements** Lucy W. Barrett, Sue Fletcher, Steve D. Wilton, 2013-06-26 There is now compelling evidence that the complexity of higher organisms correlates with the relative amount of non coding RNA rather than the number of protein coding genes. Previously dismissed as junk DNA it is the non coding regions of the genome that are responsible for regulation facilitating complex temporal and spatial gene expression through the combinatorial effect of numerous mechanisms and interactions working together to fine tune gene expression. The major regions involved in regulation of a particular gene are the 5' and 3' untranslated regions and introns. In addition pervasive transcription of complex genomes produces a variety of non coding transcripts that interact with these regions and contribute to regulation. This book discusses recent insights into the regulatory roles of the untranslated gene regions and non coding RNAs in the control of complex gene expression as well as the implications of this in terms of organism complexity and evolution **Calcium Entry Channels in Non-Excitable Cells** Juliusz Ashot Kozak, James W. Putney, Jr., 2017-07-14 *Calcium Entry Channels in Non Excitable Cells* focuses on methods of investigating the structure and function of non voltage gated calcium channels. Each chapter presents important discoveries in calcium entry pathways specifically dealing with the molecular identification of store operated calcium channels which were reviewed by earlier volumes in the *Methods in Signal Transduction* series. Crystallographic and pharmacological approaches to the study of calcium channels of epithelial cells are also discussed. Calcium ion is a messenger in most cell types. Whereas voltage gated calcium channels have been studied extensively the non voltage gated calcium entry channel genes have only been identified relatively recently. The book will fill this important niche **Regulation of Gene Expression by Small RNAs** Rajesh K. Gaur, John J. Rossi, 2009-04-27 *New Findings Revolutionize Concepts of Gene Function*. Endogenous small RNAs have been found in various organisms including humans, mice, flies, worms, fungi and bacteria. Furthermore it has been shown that microRNAs acting as cellular rheostats have the ability to modulate gene expression. In higher eukaryotes microRNAs may regulate as much as 50% of the genome **Immediate-Early Genes in the Central Nervous System** T.R. Tölle, J. Schadrack, W. Zieglgänsberger, 2012-12-06 Immediate early genes are believed to be involved in the neuron's ability to convert short term synaptic stimulation into long lasting responses and thus contribute to the adaptive alterations involved in neuronal plasticity. Cellular immediate early genes share a close structural homology with some viral oncogenes. Recent advances in cellular biology have identified the activation and deactivation of immediate early

genes as molecular mechanisms to control regulated and deregulated growth cellular differentiation and development In this view immediate early genes may function as third messengers in a stimulus transcription cascade transferring extracellular information into changes in target gene transcription thereby changing the phenotype of neurons Immediate Early Genes in the Central Nervous System provides a comprehensive up to date overview of current methodology in the research of immediate early genes and includes a wide range of neurobiological topics such as regeneration memory formation epilepsy and nociception The contributors to this book have been selected from among the leading experts in their field of research T R TOLLE J SCHADRACK W ZIEGLGANSBERGER Contents Immediate early genes how immediate and why early G Evan Immediate early gene activation as a window on mechanism in the nervous system S P Hunt L A McNaughton R Jenkins and W Wisden 18 of immediate early genes during Differential expression synaptic plasticity seizures and brain injury suggests specific functions for these molecules in brain neurons M Dragunow 35 Transcription Factors in the Nervous System Gerald Thiel, 2006-02-20 This first book to cover neural development neuronal survival and function on the genetic level outlines promising approaches for novel therapeutic strategies in fighting neurodegenerative disorders such as Alzheimer s disease Focusing on transcription factors the text is clearly divided into three sections devoted to transcriptional control of neural development brain function and transcriptional dysregulation induced neurological diseases With a chapter written by Nobel laureate Eric Kandel this is essential reading for neurobiologists geneticists biochemists cell biologists neurochemists and molecular biologists **Make Life Visible** Yoshiaki Toyama, Atsushi Miyawaki, Masaya Nakamura, Masahiro Jinzaki, 2019-10-02 This open access book describes marked advances in imaging technology that have enabled the visualization of phenomena in ways formerly believed to be completely impossible These technologies have made major contributions to the elucidation of the pathology of diseases as well as to their diagnosis and therapy The volume presents various studies from molecular imaging to clinical imaging It also focuses on innovative creative advanced research that gives full play to imaging technology in the broad sense while exploring cross disciplinary areas in which individual research fields interact and pursuing the development of new techniques where they fuse together The book is separated into three parts the first of which addresses the topic of visualizing and controlling molecules for life The second part is devoted to imaging of disease mechanisms while the final part comprises studies on the application of imaging technologies to diagnosis and therapy The book contains the proceedings of the 12th Uehara International Symposium 2017 Make Life Visible sponsored by the Uehara Memorial Foundation and held from June 12 to 14 2017 It is written by leading scientists in the field and is an open access publication under a CC BY 4 0 license *Regulation of Gene Expression in the Nervous System by Means of Alternative Splicing* Felitsiya Shakola, 2016 *Enteric Glia* Brian D. Gulbransen, 2014-07-01 The enteric nervous system ENS is a complex neural network embedded in the gut wall that orchestrates the reflex behaviors of the intestine The ENS is often referred to as the little brain in the gut because the ENS is more similar in size complexity and autonomy to the

central nervous system CNS than other components of the autonomic nervous system Like the brain the ENS is composed of neurons that are surrounded by glial cells Enteric glia are a unique type of peripheral glia that are similar to astrocytes of the CNS Yet enteric glial cells also differ from astrocytes in many important ways The roles of enteric glial cell populations in the gut are beginning to come to light and recent evidence implicates enteric glia in almost every aspect of gastrointestinal physiology and pathophysiology However elucidating the exact mechanisms by which enteric glia influence gastrointestinal physiology and identifying how those roles are altered during gastrointestinal pathophysiology remain areas of intense research The purpose of this e book is to provide an introduction to enteric glial cells and to act as a resource for ongoing studies on this fascinating population of glia Table of Contents Introduction A Historical Perspective on Enteric Glia Enteric Glia The Astroglia of the Gut Molecular Composition of Enteric Glia Development of Enteric Glia Functional Roles of Enteric Glia Enteric Glia and Disease Processes in the Gut Concluding Remarks References Author Biography Cerebellar Learning ,2014-06-07 Progress in Brain Research is the most acclaimed and accomplished series in neuroscience firmly established as an extensive documentation of the advances in contemporary brain research The volumes some of which are derived from important international symposia contain authoritative reviews and original articles by invited specialists The rigorous editing of the volumes assures that they will appeal to all laboratory and clinical brain research workers in the various disciplines neuroanatomy neurophysiology neuropharmacology neuroendocrinology neuropathology basic neurology biological psychiatry and the behavioral sciences This volume The Cerebellum and Memory Formation Structure Computation and Function covers topics including feedback control of cerebellar learning cortico cerebellar organization and skill acquisition cerebellar plasticity and learning in the oculomotor system and more Leading authors review the state of the art in their field of investigation and provide their views and perspectives for future research The volume reflects current thinking about the ways in which the cerebellum can engage in learning and the contributors come from a variety of research fields The chapters express perspectives from different levels of analysis that range from molecular and cellular mechanisms through to long range systems that allow the cerebellum to communicate with other brain areas

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