Epigenetic Regulation In The Nervous System Basic Mechanisms And Clinical Impact

The field of neuroendocrinology has extended from the initial interest in the hypothalamic control of pituitary secretion to embrace multiple reciprocal interactions between the central nervous system (CNS) and endocrine systems in the coordination of homeostasis and various physiological responses from adaptation to disease. Most recently, epigenetic mechanisms were recognized for their role in the development of the neuroendocrine axes as well as in the mediation of gene-environment interactions in stress-related psychiatry disorders.

Recent years have seen spectacular advances in the filed of epigenetics. These have attracted the interest of researchers in many fields and evidence connecting epigentic regulation to brain functions has been accumulationg. Neurons daily convert a variety of external stimuli into rapid or long-lasting changes in gene expression. A variety of studies have centered on the molcular mechanisms implicated in epigentic control and how these may operte in concert. It will be critical to unravel how specifity is achieved. The focus of this volume is on critical epigenetic regulation and chromatin remodeling events that occur in the nervous system and on the presumed mechanisms that operate within neurons to translate them into long-lasting neuronal responses.

The myelination process in the peripheral nervous system is carefully orchestrated by both transcriptional and epigenetic regulatory mechanisms. In particular, the transcription factor Early Growth response 2 (Egr2/Krox20) and associated Nab (NGFI-A/Egr-binding) corepressors are required to direct peripheral nerve myelination by Schwann cells. Furthermore, Chromodomain helicase DNA-binding protein 4 (Chd4), the core catalytic subunit of the Nucleosome Remodeling and Deacetylase (NuRD) chromatin remodeling complex interacts with Nab proteins at sites bound by Egr2. The following work examines the contributions of Chd4/NuRD to peripheral nerve myelination and delves into chromatin dynamics at cis regulatory sites both at a single myelin gene, Peripheral Myelin Protein 22 (Pmp22), and at enhancers of genes dynamically regulated during myelination. While epigenetic mechanisms play a significant role in developmental processes, specific contributions by chromatin remodeling complexes to the regulation of peripheral myelination were unexplored. In the first paper to study regulation of a specific chromatin remodeling complex in controlling peripheral nerve myelination, I generated Chd4 conditional knockout mice targeting the Schwann cell lineage (Chd4loxP/loxP; P0-cre). These mice were found to have a profound developmental myelin phenotype that includes radial sorting defects, hypomyelination, and myelin degeneration. In vivo ChIP studies reveal recruitment of Chd4 and another NuRD component, Mta2, to genes that are positively and negatively regulated by Egr2 during myelination. Further investigation into the functional role of the NuRD complex revealed a new mechanism for gene activation at Egr2 bound enhancer elements controlling expression of peripheral myelin protein 22, PMP22. Together these results implicate Chd4/NuRD as a requisite factor in timely and stable peripheral nerve myelination. To characterize active regulatory elements dynamically regulated in myelinating Schwann cells, the chromatin signature H3K27ac was assessed in mature peripheral nerve tissue and after injury-induced demyelination using ChIP-seq. The results of this study identified injury-regulated enhancer sites and transcription factors previously associated with Schwann cell myelination (Sox10, Egr2) and injury (c-Jun) as well as the novel transcriptional regulators of each condition. In total, this work expands our knowledge of the interaction between transcriptional and chromatin regulatory landscapes that define different states of Schwann cell differentiation.

Antisense RNA-Mediated Epigenetic Regulation of Brain-Derived Neurotrophic Factor..

DNA Modifications in the Brain

Chapter 11. Neuronal Genomic and Epigenetic Diversity

Epigenetics, Brain and Behavior

Chapter 7. The Mind and its Nucleosomes - Chromatin (dys)Regulation in Major Psychiatric Disease

Neural plasticity is a unique and adaptive feature of nervous system, which allows neurons to reorganize their interactions in response to a stimulation (intrinsic or extrinsic) to maintain their function. For these reasons, epigenetics emerges as a potential field for developing strategies to modulate changes in pathological situation because extrinsic factors and pharmacological tools can modify neural functioning in organisms during their life. Diet, exercise, environmental aspects, stressors or drugs are available to alter those mechanisms. Epigenetic involves certain molecular signaling pathways, as DNA methylation and histone acetylation and deacetylation, and the emerging non-coding small RNA, mainly microRNA, as a commanders of a number of translation processes. As most of molecular nervous cell alterations, epigenetic mechanisms play an important role in neural plasticity. This eBook collects the burgeoning advances in epigenetic mechanisms, focusing on new insights into cellular and molecular neurobiological mechanisms that underlie brain functioning in health and pathological conditions. Contributions go from basic cellular mechanism to therapeutic opportunities to tackle the challenges on nervous central system development and neurodegeneration.

Epigenetic Regulation in the Nervous SystemChapter 1. An Overview of the Molecular Basis of EpigeneticsElsevier Inc. ChaptersEpigenetic Regulation in the Nervous SystemBasic Mechanisms and Clinical ImpactAcademic Press

Epigenetic mechanisms (DNA modifications, histone alterations and non-coding RNAs) are crucial for transcriptional regulation and alterations of the “physiological epigenome” are increasingly associated with human diseases. During the last decade the emerging field of neuroepigenomics have started to impact tremendously in areas such learning and memory, addiction or neurodegeneration. This expert volume covers the role of epigenetic molecular mechanism in regulation of central nervous system’s function, one of the most exciting areas of contemporary molecular neuroscience. The book describes the current knowledge on the epigenetic basis of human disease covering the complete lifespan: from neurodevelopment/childhood (Rett Syndrome, Rubinstein-Taybi, autism), adolescence (eating disorders, drug addiction, anxiety), adulthood (depression, schizophrenia, amyotrophic lateral sclerosis, Huntington’s disease) and elderly (Alzheimer’s disease, Parkinson’s disease). The book also covers the three major players on neuroepigenomic mechanisms: histones alterations, DNA modifications and non-coding RNAs, their roles at the molecular and cellular level and the impact of their alterations on neuronal function and behavior. Finally, a special chapter on state-of-the-art technologies helps the reader not only to understand epigenetic driven changes in human cognition and diseases but also the methodology that will help to generate paradigm shifts on our understanding of brain function and the role of the neuroepigenome in human diseases.

Chapter 6. Drug Addiction and Reward

Epigenetic Gene Regulation in the Mammalian Central Nervous System and Its Implications in Rett Syndrome

Epigenetic Regulation of Active Enhancer Elements in Peripheral Nerve Myelination and Injury

Chapter 5. Epigenetic Mechanisms in Learning and Memory

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.

The field of neuroendocrinology has extended from the initial interest in the hypothalamic control of pituitary secretion to embrace multiple reciprocal interactions between the central nervous system and endocrine systems in the coordination of homeostasis and various physiological responses from adaptation to disease. Most recently, epigenetic mechanisms were recognized for their role in the development of the neuroendocrine axes as well as in the mediation of gene-environment interactions in stress-related psychiatry disorders.

DNA Modifications in the Brain: Neuroepigenetic Regulation of Gene Expression begins with an historical overview of the early discoveries surrounding DNA methylation in the mammalian brain and then explores the evidence supporting a role for this epigenetic mechanism in controlling gene expression programs across the lifespan in both normal and diseased states. Chapters describe new directions and technological advances, and provide an overview of what the future holds for this exciting new field. This book is ideal for medical, graduate and advanced undergraduate students, but is also a great resource for researchers who need a broad introduction to the dynamic nature of DNA that sheds light on evolving concepts of gene-environment interaction and their effects on adaptation and neuropsychiatric disease. Provides a comprehensive overview of the many facets of DNA modifications Discusses the impact of this dynamic epigenetic mechanism across brain development and lifespan at behavioral, cognitive, molecular and genetic levels Contains contributions by influential leaders in the field Edited by a Neuroscientist to further promote synthesis between epigenetics, neuroscience, and clinical relevance

Epigenetics of Chronic Pain

Basic Mechanisms and Clinical Impact

Evaluation of the Epigenetic Regulation of Two X-linked, Autism Candidate Genes: X-linked Lymphocyte Regulated 3b and Transketolase-Like 1

Regulation of Gene Expression in the Drosophila Olfactory System Varies Widely with Stimulus, Duration, Age, and Development

Chapter 14. Epigenetics: Defining the Frontiers of Genomic Function

Long noncoding RNAs (lncRNAs) regulate chromatin remodeling through their interactions with epigenetic enzymes during development and disease. The inhibition of the natural antisense transcript of Brain-derived neurotrophic factor (BDNF-AS), results in BDNF promoter de-repression and transcriptional upregulation, both in vitro and in vivo. Recently, we showed that BDNF-AS interacts with the histone methyltransferase enhancer of zeste homolog 2 (EZH2) to suppress BDNF mRNA and protein expression. BDNF is an important neurotrophin that is required for neural development and maintenance of the nervous system. Dysregulation of BDNF occurs in a number of neurological disorders, including: Alzheimer's Disease, Parkinson's Disease, Rett syndrome, and amyotrophic lateral sclerosis. Previous attempts to upregulate BDNF by administering the recombinant form in various parts of the central nervous system have failed, mostly due to the challenge of delivering BDNF to the correct cells and neural networks. Our approach to upregulating BDNF by modulating its interaction with an epigenetic enzyme is a highly specific target with potential therapeutic value. To achieve this, we developed a novel pharmacological assay to characterize the interaction between long noncoding RNAs and their epigenetic targets using Amplified Luminescent Proximity Homogeneous Assay (AlphaScreen) technology. With this assay, we are able to quantify lncRNA-protein interactions rapidly for the purpose of high throughput screening, enabling drug discovery efforts for this novel class of drug targets. In this work, we present our assay development and screening findings, including the identification of potential small molecule modulators of lncRNA-protein interactions. Furthermore, we describe the application of this lncRNA-protein interaction assay to detect RNA requirements for EZH2 recruitment, a much debated and important question that lingers in the field. From our work, it is evident that BDNF-AS has several regions of RNA that are required for EZH2 recruitment, potentially due to the importance of this transcript in regulating BDNF. This work describes exploratory drug discovery for a novel class of drug targets as well as applications to understand the basic biochemistry governing lncRNA-protein interactions.

Epigenetics is the study of heritable changes in gene function that do not involve changes in the DNA sequence. These changes, consisting principally of DNA methylation, histone modifications, and non-coding RNAs, maintain or modulate the initial impact of regulatory factors that recognize and associate with particular genomic sequences. Epigenetic modifications are manifest in all aspects of normal cellular differentiation and function, but they can also have damaging effects that result in pathologies such as cancer. Research is continuously uncovering the role of epigenetics in a variety of human disorders, providing new avenues for therapeutic interventions and advances in regenerative medicine. This book's primary goal is to establish a framework that can be used to understand the basis of epigenetic regulation and to appreciate both its derivation from genetics and interdependence with genetic mechanisms. A further aim is to highlight the role played by the three-dimensional organization of the genetic material itself (the complex of DNA, histones and non-histone proteins referred to as chromatin), and its distribution within a functionally compartmentalized nucleus. This architectural organization of the genome plays a major role in the subsequent retrieval, interpretation, and execution of both genetic and epigenetic information.

According to the CDC the prevalence of Autism Spectrum Disorder (ASD) in males compared to females is approximately 5:1. Skuse and others hypothesized that imprinted genes on the X chromosome could account for this sex bias. Genomic imprinting is defined as differential gene expression dependent upon the parental origin of the allele. While genomic imprinting on autosomes has been well classified, no imprinting mechanism on the sex chromosomes has been discovered. This work presents an investigation into the regulation of expression governing the imprinted locus of X-Linked Lymphocyte Regulated 3b/4b/4c (Xlr3/4), and closely linked ASD candidate gene, Transketolase-Like 1 (TKTL1), in the developing central nervous system of the laboratory mouse. Examination of epigenetic signatures and the chromatin environment including differential DNA methylation, differential nucleosome positioning, H3.3 deposition and G-quadruplex formation, suggests that epimutations in these loci may underlie disease association. Transketolases play a pivotal role in the Pentose Phosphate Pathway (PPP), and dysfunction in the non-oxidative phase of the PPP has been linked to neurodegenerative disorders and cancers. This work explores the expression of TKTL1 in human brain sub-regions of ASD patients compared to neurotypical individuals as well as the functional role TKTL1 plays in the PPP. It is observed that TKTL1 may not function as a transketolase in the pathway, but may play a critical regulatory role as a competitive inhibitor.

Chapter 1. An Overview of the Molecular Basis of Epigenetics

Chapter 12. Adult Neurogenesis

Brain, Behavior and Epigenetics

Chapter 2. Histone Modifications in the Nervous System and Neuropsychiatric Disorders

Epigenetic Mechanisms in Neural Plasticity

Epigenetics in Psychiatry, Second Edition covers all major areas of psychiatry in which extensive epigenetic research has been performed, fully encompassing a diverse and maturing field, including drug addiction, bipolar disorder, epidemiology, cognitive disorders, and the uses of putative epigenetic-based psychotropic drugs. Uniquely, each chapter correlates epigenetics with relevant advances across genomics, transcriptomics, and proteomics. The book acts as a catalyst for further research in this growing area of psychiatry. This new edition has been fully revised to address recent advances in epigenetic understanding of psychiatric disorders, evoking data consortia (e.g., CommonMind, ATAC-seq), single cell analysis, and epigenome-wide association studies to empower new research. The book also examines epigenetic effects of the microbiome on psychiatric disorders, and the use of neuroimaging in studying the role of epigenetic mechanisms of gene expression. Ongoing advances in epigenetic therapy are explored in-depth. Fully revised to discuss new areas of research across neuronal stem cells, cognitive disorders, and transgenerational epigenetics in psychiatric disease Relates broad advances in psychiatric epigenetics to a modern understanding of the genome, transcriptome, and proteins Catalyzes knowledge discovery in both basic epigenetic biology and epigenetic targets for drug discovery Provides guidance in research methods and protocols, as well how to employ data from consortia, single cell analysis, and epigenome-wide association studies (EWAS) Features chapter contributions from international leaders in the field

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

The mammalian nervous system is a highly intricate network consisting of over a hundred billion specialized cells called neurons. One unique characteristic of neurons is their highly polarized morphology; unlike other cells, neurons project long axonal extensions. These structures allow them to connect and communicate with not only other neurons, but also various cell types in the body and give rise to all motor, sensory, and higher order function. Because axons can extend up to three feet, they are also vulnerable to injury from sources such as traumatic brain and spinal cord injuries, stroke, or neurodegenerative diseases. Indeed, patients who have experienced these injuries often suffer debilitating, irreversible loss of function. Interestingly, whereas neurons which reside in the central nervous system are incapable of regenerating after axon injury, neurons of the peripheral nervous system activate a robust pro-regenerative response capable of promoting long distance regeneration and functional recovery. The molecular mechanisms which underlie this pro-regenerative response may provide key insights into how a pro-regenerative response could be stimulated in injured central nervous system neurons. A comprehensive overview of the known molecular mechanisms involved in this response is reviewed in Chapter 1.As mammals age, the synaptic connections between neurons mature. Following axon injury in peripheral nervous system neurons, the genes involved in synaptic function are turned off and genes required for inducing axon growth are activated. These widespread epigenetic and transcriptional changes require a coordinated effort of epigenetic and transcriptional regulators including epigenetic modifiers, transcription factors, and microRNAs. In Chapter 2, we demonstrated that these changes are, in part, a result of the rapid downregulation of microRNA-9 which occurs following axon injury. At baseline in adult peripheral nervous system neurons, microRNA-9 is highly expressed and actively represses various genes including REST and UHRF1. When microRNA-9 expression decreases following injury, both REST and UHRF1 increase with UHRF1also repressing REST and restricting REST expression to a tight temporal window. During this time, REST binds to and represses various genes involved in synaptic function such as ion channels; a process necessary for peripheral nervous system regeneration. This complete published work can be found in Chapter 2.In coordination with epigenetic modifiers such as UHRF1, various transcription factors are activated following axon injury and promote the expression of pro-growth genes. Various studies have worked to identify the transcription factors involved in this process as exogenous overexpression of transcription factors has been shown to confer specific phenotypes of interest, such as the conversion of one cell type to another, when the correct combination of transcription factors is manipulated. To further this work, in Chapter 3 I used bioinformatics analysis to identify 27 transcription factors putatively involved in the establishment of the pro-regenerative response. Using two complimentary in vitro screens, determined which transcription factors were both necessary for peripheral nervous system axon regeneration and sufficient to drive central nervous system axon regeneration. By pairing these results with network-based bioinformatics analysis, we identified Creb1 as a transcription factor which sits atop the pro-regenerative gene regulatory network. Follow-up studies in which we overexpressed Creb1during optic nerve regeneration demonstrated Creb1 is sufficient to promote central nervous system axon regeneration in vivo. This work provides exciting new insight into the various transcription factors regulating this response as well as their putative genetic relationships.

Epigenetics and Neuroendocrinology

Chapter 9. miRNAs and Neurodevelopmental Disorders

With implications of epigenetic regulation and genetic architecture for human development and health

Neuroepigenetic Regulation of Gene Expression

Genomics, Proteomics, and the Nervous System

Biomedical research in the first decade of the 21st century has been marked by a rapidly growing interest in epigenetics. The reasons for this are numerous, but primarily it stems from the mounting realization that research programs focused solely on DNA sequence variation, despite their breadth and depth, are unlikely to address all fundamental aspects of human biology. Some questions are evident even to non-biologists. How does a single zygote develop into a complex multicellular organism composed of dozens of different tissues and hundreds of cell types, all genetically identical but performing very different functions? Why do monozygotic twins, despite their stunning external similarities, often exhibit significant differences in personality and predisposition to disease? If environmental factors are solely the cause of such variation, why are similar differences also observed between genetically identical animals housed in a uniform environment? Over the last couple of decades, epigenetics has undergone a significant metamorphosis from an abstract developmental theory to a very dynamic and rapidly developing branch of molecular biology. This volume represents a compilation of our current understanding about the key aspects of epigenetic processes in the brain and their role in behavior. The chapters in this book bring together some of the leading researchers in the field of behavioral epigenetics. They explore many of the epigenetic processes which operate or may be operating to mediate neurobiological functions in the brain and describe how perturbations to these systems may play a key role in mediating behavior and the origin of brain diseases.

Proper cellular development and function is a complex process established by elaborate gene expression networks. These networks are regulated by epigenetic processes, which alter chromatin states and coordinate the binding of transcription factors (TFs) to regulatory elements (REs), such as enhancers, across the genome to facilitate gene expression. It follows then that a major experimental effort is to profile and understand the binding patterns of TFs to REs in various cellular types and contexts. Critically however, current TF profiling techniques are limited in their abilities to profile TF occupancy in targeted cellular populations and temporal windows, hindering investigations into epigenetic control in complex, multicellular systems, such as the brain. This dissertation focuses on two related areas: firstly, the design of new tools for profiling TF genome occupancy in the mouse brain in specific cellular populations and time periods, and secondly, investigating TF-mediated mechanisms of disease pathogenesis in animal models. In Chapter 2, we describe the development of a novel, viral-mediated method, termed adeno-associated virus (AAV) calling cards, for profiling binding sites of TFs across the genome in the live mouse brain. The AAV calling cards approach allows unique access to TF occupancy information that is inaccessible with other existing techniques, including cell type specificity (through Cre-mediated conditional expression) and historical binding (through longitudinal occupancy recording). Then, in Chapters 3 and 4, we apply this new technique to mouse models to investigate epigenetic misregulation in disease. Previous studies have demonstrated that a large portion of genetic variation associated with cellular dysfunction or disease exists in TF-bound enhancers, demonstrating the criticality of proper TF binding in maintaining cellular homeostasis. However, whether these elements are misregulated more broadly in disease contexts is unclear. In Chapter 3, we apply AAV calling cards to a model of acute seizure and uncover aberrant epigenetic regulation which is predictive of phenotypic outcomes. Particularly important in this study is the ability of AAV calling cards to record and integrate historical TF binding information, allowing linkage of antecedent epigenetic events to eventual seizure outcomes. Here, we longitudinally recorded prodromal enhancer activity to identify loci which are predictive of seizure severity. Next, in Chapter 4, we investigate epigenetic regulation in animal models and postmortem tissues from individuals with amyotrophic lateral sclerosis (ALS). In this study, we focus on a subset of ALS caused by a large hexanucleotide (G4C2) repeat expansion in the gene chromosome 9 open reading frame 72 (C9orf72), which is the most common genetic cause of ALS (C9ALS). Utilizing AAV calling cards as well as other established epigenomic profiling techniques, we observe broad epigenetic misregulation both in C9ALS mouse models and human tissues at the transcriptional and translational levels. Importantly, the C9ALS mouse models used in this study do not develop motor neuron degeneration or ALS-like phenotypes and were profiled at an early age, suggesting that these changes occur early in the disease process and are likely driven by C9orf72-related pathologic species, such as dipeptide repeat proteins (DPRs). Finally, in Chapter 5 we investigate the characteristic properties of C9orf72-specfic pathologies, including DPRs, in human C9ALS. We probed size and abundance of DNA expansions and DPRs in blood, cerebrospinal fluid, and postmortem tissues from C9ALS and sporadic ALS (sALS) individuals and identified novel correlations of C9ALS patient pathologies with clinical and demographic data. Moving forward, these data will facilitate mechanistic studies and clinical trials aimed at reducing or altering C9ALS pathologies in the central nervous system (CNS). In summary, the body of work detailed here extends our knowledge of TFs in both the healthy and diseased central nervous system (CNS), providing new insights into the role of epigenetic regulation in disease pathogenesis. Further, the establishment of AAV calling cards as a widely applicable epigenomic tool will empower innovative new studies in a variety of tissue and model systems.

Computational Epigenetics and Diseases, written by leading scientists in this evolving field, provides a comprehensive and cutting-edge knowledge of computational epigenetics in human diseases. In particular, the major computational tools, databases, and strategies for computational epigenetics analysis, for example, DNA methylation, histone modifications, microRNA, noncoding RNA, and ceRNA, are summarized, in the context of human diseases. This book discusses bioinformatics methods for epigenetic analysis specifically applied to human conditions such as aging, atherosclerosis, diabetes mellitus, schizophrenia, bipolar disorder, Alzheimer disease, Parkinson disease, liver and autoimmune disorders, and reproductive and respiratory diseases. Additionally, different organ cancers, such as breast, lung, and colon, are discussed. This book is a valuable source for graduate students and researchers in genetics and bioinformatics, and several biomedical field members interested in applying computational epigenetics in their research. Provides a comprehensive and cutting-edge knowledge of computational epigenetics in human diseases Summarizes the major computational tools, databases, and strategies for computational epigenetics analysis, such as DNA methylation, histone modifications, microRNA, noncoding RNA, and ceRNA Covers the major milestones and future directions of computational epigenetics in various kinds of human diseases such as aging, atherosclerosis, diabetes, heart disease, neurological disorders, cancers, blood disorders, liver diseases, reproductive diseases, respiratory diseases, autoimmune diseases, human imprinting disorders, and infectious diseases

Chapter 8. HDAC Inhibitors as Novel Therapeutics in Aging and Alzheimer’s Disease

Clinical Focus on Psychiatry, Volume 2

Epigenetics, Nuclear Organization & Gene Function

Regulation of Gene Expression in the Nervous System

Chapter 13. Transgenerational Inheritance in Mammals

The book aims to provide an overview of current knowledge regarding epigenetics and epigenomics. Included are reviews on the role of epigenetics in the development and pathogenesis of the vascular endothelium and nervous system, as well as our current understanding of the potential etiologies of Autism Spectrum Disorders. Additional chapters are devoted to DNA methylation, genomic imprinting and human reproduction. A discussion of the role of the epigenome in cancer prevention and polyphenols is also included. Authors provide research findings from both human data and animal model studies. This book will be of interest to scientists, physicians and lay readers wishing to review recent developments in the field of epigenetics and epigenomics.

Epigenetic Biomarkers and Diagnostics comprises 31 chapters contributed by leading active researchers in basic and clinical epigenetics. The book begins with the basis of epigenetic mechanisms and descriptions of epigenetic biomarkers that can be used in clinical diagnostics and prognostics. It goes on to discuss classical methods and next generation sequencing-based technologies to discover and analyze epigenetic biomarkers. The book concludes with an account of DNA methylation, post-translational modifications and noncoding RNAs as the most promising biomarkers for cancer (i.e. breast, lung, colon, etc.), metabolic disorders (i.e. diabetes and obesity), autoimmune diseases, infertility, allergy, infectious diseases, and neurological disorders. The book describes the challenging aspects of research in epigenetics, and current findings regarding new epigenetic elements and modifiers, providing guidance for researchers interested in the most advanced technologies and tested biomarkers to be used in the clinical diagnosis or prognosis of disease. Focuses on recent progress in several areas of epigenetics, general concepts regarding epigenetics, and the future prospects of this discipline in clinical diagnostics and prognostics Describes the importance of the quality of samples and clinical associated data, and also the ethical issues for epigenetic diagnostics Discusses the advances in epigenomics technologies, including next-generation sequencing based tools and applications Expounds on the utility of epigenetic biomarkers for diagnosis and prognosis of several diseases, highlighting the study of these biomarkers in cancer, cardiovascular and metabolic diseases, infertility, and infectious diseases Includes a special section that discusses the relevance of biobanks in the maintenance of high quality biosamples and clinical-associated data, and the relevance of the ethical aspects in epigenetic studies

This newest volume of Advances in Neurobiology discusses the utilization of genomic and proteomic technologies, to address facets of neurobiology including development and epigenetic regulation, functions in learning and memory, and changes associated with neurological and psychiatric disorders.

Epigenetics and Epigenomics

Transcription Factor-mediated Epigenetic Regulation in the Healthy Brain and Neurological Disease

Epigenetics in Psychiatry

Neuroepigenomics in Aging and Disease

Computational Epigenetics and Diseases

Epigenetics of Chronic Pain, Volume Nine, presents comprehensive information on the role of epigenetics in chronic pain sensitivity, providing a detailed, but accessible, view of the field from basic principles, to clinical application. Leading international researchers discuss essential mechanisms of chronic pain epigenetics, including the molecular processes of chromatin remodeling, histone modifications, and the microRNAs and noncoding RNAs involved in regulating genes tied to pain sensitivity. The influence of epigenetics in inflammatory, neuropathic, visceral and other pain models is examined, with data derived from epigenetic studies on peripheral and central mechanisms of pain sensitivity in animal models and clinical cases studies. The studies and case examples cited highlight therapeutic pathways of significance and next steps for researchers to develop epigenetic-based treatments for chronic pain. In recent years, epigenetic regulation of gene expression has been shown to play a central role in managing human pain sensitivity. Findings show that expression of many genes critical to increases or decreases in pain sensitivity are indeed regulated by DNA methylation and its enzymes, histone-involved chromatin remodeling, and noncoding RNAs, mainly microRNAs. Compiles all known information on epigenetic regulation of chronic pain in one volume Covers the basic functionality of epigenetic mechanisms involved in pain management, applications of recent research in understanding different types of chronic pain, and pathways for developing therapeutics Leading international researchers from across academia, clinical settings, and the pharmaceutical industry discuss epigenetics in inflammatory, neuropathic, visceral, and other pain models in-depth Enables clinicians, researchers, and pharmacologists to better understand and treat chronic pain

The Drosophila olfactory system is an ideal model for the investigation of principles of gene regulation in the nervous system. Within this system, we characterize gene expression changes in response to short-term and long-term exposure to odorants. Additionally, we examine the contributions of two transcription factors to the development of this chemosensory system. Short-term exposure to odorants and light leads to neural activation and induction of activity regulated genes (ARGs). ARG induction in neurons in can lead to long-term changes at the level of the synapse. Such alterations in synaptic structure/function are thought to underlie important cellular processes such as synaptic plasticity and long-term memory formation. We have conducted a genome-wide study of genes in the Drosophila central nervous system induced after brief periods of sensory stimulation and have identified 352 genes whose ix expression increases in response to neural activity. The regulation of these genes is altered with increasing age. Furthermore, we demonstrate that loss of a histone deacetylase alters neuronal response to sensory stimuli, suggesting a mechanism of epigenetic regulation. We extended our transcriptome analysis to the fly antenna and found that the genes increased in response to fruit odorants differ significantly from the genes induced by the repellent DEET. In response to long-term exposure to the odorant diacetyl, we find that dramatic changes in gene expression can, in part, be attributed to inhibition of histone deacetylases. This non-traditional action of diacetyl slows neurodegeneration in the fly model for Huntington's Disease. We conclude with an analysis of two transcription factors acj6 and pdm3 and find they regulated proper chemosensory receptor and axon guidance gene expression in the developing Drosophila olfactory system.

Chapter 3. Active DNA Demethylation and 5-Hydroxymethylcytosine

Epigenetic Gene Regulation in Mouse Embryonic Stem Cells and the Developing Central Nervous System

Transcriptional and Epigenetic Regulation of Axon Regeneration

Clinical Focus on Psychiatry, Volume 1

Epigenetic Regulation of Oligodendrocyte Development and Regeneration in the Central Nervous System