The Nuclear Receptor Superfamily

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Androgens and Androgen Receptor Mechanisms, Functions and Clinical Applications

The first edition of "Testosterone: Action, Deficiency, Substitution" was published in 1990. Since then our understanding of the hormone that turns males into men has tremendously increased. Therefore, the editors felt that a second extended edition of the book is warranted in order to summarize established and recent findings in the field and to present the reader with an up-to-date reflection by the textbook. The increased mass of knowledgegrowth of the volume from 14 to 20 chapters. In the updated edition the biochemistry and metabolism of androgens have been complemented by extensive information on the molecular biology of the androgen receptor and its disorders. The key role of testosterone in spermatogenesis is now better defined. We have a more complete understanding of the psycho-pi effects of testosterone and know so much about the different target organs and functions that individual chapters deal with testosterone and the prostate, lipids and the cardiovascular system, hair, bones and muscles.

The general chapter on pharmacology and clinical uses of testosterone, in particular in male hypoandrogenism, is extended by pharmacokinetic studies on testoster one preparations and individual substitution modalities using testosterone esters as well as implants and advanced transdermal applications. The physiologic basis and possible clinical applications of testosterone in non-gonadal diseases, in male senescence, in male hormonal contraception and in transsexuals are discussed. The last chapter describes the role of "investigative" steroid biochemistry applied to tracking anabolic steroid abuse.

Modulation of Androgen Receptor Activity by P160 Coactivators and a Study of Environmental Contaminants

Updated with new and expanded chapters, Endocrine Disruption and Human Health, Second Edition provides an introduction to what endocrine disruptors are, the issues surrounding them, the source of these chemicals in the ecosystem and the mechanisms of action and assay systems. Contributions by specialists are included to discuss the varying effects of endocrine disruption on human health, including effects on development and reproduction, effects on the immune system and endocrine disruption and cancer. New chapters on epigenetic mechanisms of action and risk assessment of endocrine disruptors, and current approaches to their regulation are also covered. With new material on topics such as medium-term, low dose mixtures, windows of susceptibility, epigenetics, EDCs effect on the gut microbiome, EDCs in from polluted air and oral exposures, green chemistry, and nanotechnology, the new edition of Endocrine Disruption and Human Health is a valuable and informative text for academic and clinical researchers and other health professionals approaching endocrine disruption and its effects on human health for the first time, graduate students, and advanced undergraduate students. Provides readers with access to a range of information from the basic mechanisms and assays through to cutting-edge research investigating concerns for human health. Presents a comprehensive, translational look at all aspects of endocrine disruption and its effects on human health. Offers guidance on the risk assessment of endocrine disruptors and current relevant regulatory considerations. Newly added content on topics like late-term, low dose mixtures, windows of susceptibility to EDCs, EDCs effect on the gut microbiome, green chemistry, and nanotechnology.

Advances in Testosterone Action

The book provides chapters on sex hormones and their modulation in neurodegenerative processes and pathologies, from basic molecular mechanisms, physiology, gender differences, to neuroprotection and clinical aspects for potential novel pharmacotherapy approaches. The book contains 14 chapters written by authors from various biomedical professions, from basic researches in biology to medicine and veterinary medicine, pharmacologists, psychologists, etc. Chapters sum up the past and current knowledge on sex hormones, representing original new insights into their role in brain functioning, mental disorders and neurodegenerative diseases. The book is written for a broad range of audience, from biomedical students to highly profiled medical specialists and biomedical researchers, helping them to expand their knowledge on sex hormones in neurodegenerative processes and opening new questions for further investigation.

Androgens and Androgen Receptor

In the past 10 years hirsutism has been the object of a considerable number of fundamental studies. It provides endocrinologists with an experimental model for the investigation of androgen secretion, metabolism and mechanism of action. Plasma androgen assay, free testosterone measurement, hepatic and extrahepatic androgen metabolic clearance and androgen metabolism in the skin are the different steps which were studied by many groups and represent valuable parameters of the mechanisms of hirsutism. Determination of the origin of androgens oversecretion has become easier by technical progress in differential effluent venous catheterization, which makes it possible to compare androgens in differential effluent venous catheterization and androgens in peripheral levels, and to determine the ovariad arterial source of the androgen oversecretion as well as the side responsible, essential in the case of tumors. The study of androgen metabolism and the discovery of androgen receptors in the human skin confirm the latter as an actual target cell for androgens. This target cell uses the circulating active androgens, i.e., testosterone and can also metabolize local inactive androgens into active ones. This is the case of androstenedione and dehydroandrosterone which are the two main androgens secreted in women, since women secrete very little testosterone. The capacity of the skin to transform inactive androgens into active ones varies from one individual to another. That would support the concept of variable skin receptivity from one woman to another and from one ethnic group to another.

Sex Steroids and Apoptosis in Skeletal Muscle: Molecular Mechanisms
Hormones, Cognition and Dementia

Insight into the role of hormones, particularly estrogen and testosterone, in health and disease etiology - including interactions with other hormone pathways - has dramatically changed. Estrogen and androgen receptors, with their polymorphisms, are key molecules in all tissues and are involved in a number of homeostatic mechanisms but also pathological processes including carcinogenesis and the development of metabolic and neurological disorders such as diabetes and Alzheimer’s disease. Endocrine disrupting chemicals (EDCs) can interfere with the endogenous hormone systems at certain dosages and play a key role in the pathology of disease. Most known EDCs are mammified and are therefore an increasing concern given the number commonly found in household products and the environment. This book will cover the mechanisms of EDC pathologies across the spectrum of disease, as well as risk assessment and governmental regulation to provide a holistic view of the current issues and cutting-edge research in the topic. With contributions from global leaders in the field, this book will be an essential reference for toxicologists, endocrinologists and researchers interested in developmental biology, regulatory toxicity and the interface between environment and human health.

Effects of Testosterone on Proliferation, Differentiation and Androgen Receptor Content of Porcine Satellite Cells in Vitro

Introduction to androgens was neither auspicious nor impressive. I was sitting my viva voce examination for a degree in physiology and had haltingly intimated to my examiner (name decorously withheld) that I intended to pursue a career in research. “On what topic?” was the reply. I had been deeply impressed by the work of C. Huggins and C. V. Hges (Cancer Res. 1, 293, 1941) on the dramatic arrest of canine prostatic hyperplasia by the administration of stilbostrol. With some enthousiasm, I responded, “On steroid hormones, because I am struck by the profound effects that may be achieved by relatively small numbers of molecules.” The examiner sank into deep contemplation before replying, “By young man, have you considered going into teaching?” Suitably chastened, I finally began my research career investigating the effects of steroids on the nucleic acid metabolism of experimental tumours and on the process of cell division. Reaching an impasse in this work, I mentioned one of meseness animal’s day to Dr. G. F. Marian that, somewhat surprisingly, we had no understanding of the fundamental mechanism of action of steroid hormones, especially the androgens. To tackle this problem, particularly since exciting new insights in androgens encouraged me then being made into the interaction of radioactively labelled oestradiol-17B with such tissues as rat uterus.

Receptors and Hormone Action

A practical approach to the field of androgen excess or deprivation in women’s health. The content includes multiple viewpoints on the most common disorders in this class, including polycystic ovary disease, hirsutism and menopausal issues. Each chapter provides a combination of long-lasting clinical principles in the diagnosis and management of these patients along with a state-of-the-art review. This text takes an innovative approach to uncommon conditions (such as congenital adrenal hyperplasia, transgender conditions). In addition to presenting clinical insights, and a review of the basic science underpinning these conditions, it focuses on key concepts that can be derived from these rare conditions to the entire field. This book is an essential addition to the library for any busy clinician who is looking for a practical reference guide but also for the sub-specialist who is looking for new and thought-provoking insights in this complex scientific area.

Challenges in Endocrine Disruptor Toxicology and Risk Assessment

Androgens are critical for the development and maintenance of adult male characteristics such as muscle mass and sexual function. Consequently, the established decline with age of serum testosterone (T) in males has major health implications. While the androgen receptor (AR) is the major mediator of genomic androgen action and is required for the development of the male phenotype, reproductive organs and the maintenance of male secondary sexual characteristics, it is the entrance of androgens into the cell that mediates the activation of the AR and the subsequent modulation of androgen-regulated genes. The objectives of this thesis were to develop a specific mammalian cell-based bioassay capable of reliably measuring T in serum and to determine the ability of this bioassay to measure a physiologically relevant fraction of T in serum. Additionally, this thesis aimed to determine the relative contributions and roles of the activation functions of the AR to overall AR transcriptional activity along with the functional contributions for AR signalling of prostate cancer mutations which have previously been identified in the AF5 region of the AR NTD. The investigation of the roles of the activation functions in the AR in this thesis have revealed that while the AF1 domain is responsible for the majority of the transcriptional activity of the AR, AFS and AF2 govern the sensitivity and cellular response of the AR to androgens by providing protein and interdomain interaction interfaces. Furthermore, the evidence in this thesis demonstrates that the AR requires interdomain communication for sensitive AR signalling. Finally, the findings in this thesis demonstrate that the AF5 surface is required for the N/C interaction and coregulator interactions while advanced prostate cancer mutations identified within this region confer increased transcriptional activity of the AR in the presence of high levels of cellular steroids. Collectively, the findings in this thesis provide several novel insights into the mechanism of action of serum androgens and challenges several long held assumptions of androgenic action in males. These findings also delineate a mechanism of treatment failure in advanced prostate cancer, provide a novel model for the events leading to sensitive AR transactivation and contribute to the understanding of physiologically relevant levels of serum T.

The effects of androgens on steroidogenesis in the ovary of Atlantic croaker (Micropogonias undulatus)

While menopause in women is a well-established and well-documented phenomenon, the andropause in men is a relatively new concept. The terms male menopause and andropause suggest that this is an abrupt phenomenon related to a sudden deprivation of sex hormones. Unlike the menopause, which has a relatively sudden onset, the andropause appears to be a gradual process. It has been hypothesized that an androgen deficiency might develop with aging. Androgens and the A-R M. A. Malle explores this hypothesis. The book focuses on the gradually progressive problems related to the decline in androgens which occur with advancement of age. I examine the debate about the extent to which an age-dependent decline in androgens leads to health problems that affect or impair the quality of life, and the theory behind it. In addition, it reviews studies evaluating the effects of androgen supplementation. Androgens and the A-R M. A. Malle comprehensively covers androgen function and how it changes over time.

M androgen-Induced Transactivation of the Androgen Receptor as a Molecular Mechanism for Prostate Cancer Development

A new paradigm that has gradually transformed larger, terminal hair follicles in some scalp regions of genetically susceptible individuals into small, non-hairy ones, resulting in male pattern baldness. Androgens are believed to act on the main epithelial hair follicle via the androgen-receptor-mediated derived papilla. The aim of this study was to establish the culture of dermal papilla cells derived from balding scalp hair follicles and to investigate the mechanisms of androgen action in dermal papilla cells derived from balding and non-balding scalp in an attempt to understand how androgens inhibit terminal hair follicles. Dermal papilla cells from balding scalp non-follicles were considerably smaller and hence more difficult to culture than those from non-balding scalp. Primary dermal papilla cell lines derived from balding scalp showed several differences in vitro compared with those from non-balding scalp. Saturation analysis revealed the presence of high affinity, low capacity androgen receptors in all cell types, with balding scalp showing several differences in vitro compared with those from non-balding scalp. Competition studies confirmed the androgen specificity of these receptors. A putative, novel androgenic receptor was unable to compete for the androgen receptor. Although the androgenic receptor was unable to direct proliferation of the growth of dermal papilla cells in vitro, it had a significant effect on the growth of dermal papilla cells in vivo, probably in part due to the increased concentration of T in serum. Androgenic receptor were able to induce the production of factors which inhibited the growth of the continuous epithelial cell line, NCTC 2544. Cultured dermal papilla cells clearly exhibit an altered gene expression which is reflective of the effect on in vivo origins and therefore appear to offer an excellent model system to study the effects of androgen on hair growth.

Endocrinology of the Testis and Male Reproduction
Androgens in Prostate Cancer

New developments in testosterone therapy are summarized here by internationally renowned experts. They review both basic and clinical knowledge in fourteen chapters. The book begins with the biochemistry of testosterone, its biosynthesis, metabolism and mechanisms of action in target organs. Three chapters deal with specific aspects of testosterone action, namely its role in spermatogenesis, its psychotropic effects and its effects on bones. Syndromes caused by androgen resistance are described in order to highlight the importance of properly functioning enzymes and receptors in the target organs. Causes and symptoms of male hypogonadism, the major indication for testosterone treatment, are described. Five chapters are devoted to the pharmacology, pharmacokinetics and clinical uses and abuses of testosterone preparations. The new therapeutic testosterone application is described in detail. Side effects of testosterone treatment are reviewed. The possible role of androgens in the development of prostatic hyperplasia and carcinoma is discussed extensively since this question is of major concern to the clinician.

Androgens in Gynecological Practice

The subject of this book is neuroendocrinology, that branch of biological science devoted to the interactions between the two major integrative organ systems of animals—the endocrine and nervous systems. Although this science today reflects a fusion of endocrinology and neurobiology, this synthetic ap proach is relatively recent. At the beginning of the 20th century, when the British physiologists, Bayliss and Starling, first proposed endocrinology to be an independent field of inquiry, they went to great lengths to establish the autonomy of chemical secretions in general and their independence from nervous control in particular (Bayliss, W. H., and Starling, E. H., 1902. The mechanism of pancreatic secretion. J. Physiol. 28:325). They argued with Pavlov, who said that there was a strong influence of the nervous system on the gastro-intestinal phenomena the endocrinologists were studying. For several decades, the English physiologists prevailed, at least in the West; and Pavlov's critique was not taken to heart by the practitioners of the newly emerging discipline of endocrinology. Through the work of Harris, the Scharrers, Sawyer, Everett, and others, there has been something of a scientific detente in the latter half of this century; the hybrid field of neuroendocrinology is now regarded as one of the corner stones of modern neural science and is of fundamental importance in basic and clinical endocrinology.

Neuroendocrinology of Reproduction

Oxidative stress-associated neurodegenerative diseases, such as Parkinson's disease (PD), affect millions of people worldwide. Although aging is the greatest risk factor for PD, other significant factors may be implicated, such as sex hormones that can mediate sex differences. Men have a higher incidence and prevalence of PD than women. Therefore, testosterone, a primary male sex hormone and a known oxidative stressor, is implicated in PD pathophysiology. Since androgens can have negative effects on dopaminergic cells, it is imperative to understand the underlying mechanisms in order to determine what mediates the observed sex differences in PD prevalence. NADPH Oxidase 1 and 2 are major oxidative stress generators in the brain, thus potential targets for testosterone-induced oxidative stress and cell death. This dissertation project therefore investigates the role of androgens and membrane androgen receptor activation on NADPH oxidase 2. The findings of this study help identify key players in testosterone-induced neurodegeneration, which could serve as potential therapeutic targets for PD. Ultimately, this project provides novel mechanisms to explain thought provoking questions on male sex bias in PD.

Endocrine Disruption and Human Health

This book describes recent findings on androgens. The chapters include information on physiological and pathological conditions such as alteration in testosterone production by Leydig cells, prostate cancer, and metabolic disorders. Moreover, this book refers to the potential use of androgens in assisted human reproduction treatments and bovine breeding. Since each chapter contains background information based on evidence and emphasizes basic science, this book is aimed at professionals who already have a basic understanding of the principles of androgen biochemistry and endocrine-related diseases.

The Androgen Receptor

This monograph focuses on the actions exerted by sex hormones, 17β-estradiol and testosterone, in skeletal muscle tissue. An important consideration of this volume is the fact that both estrogen receptors (ERs) and androgen receptors (ARs) are ubiquitously expressed and, as a result, steroid hormones affect growth and different cell functions in several organs. Moreover, ERs and ARs may have a non-classical pattern of intracellular localizations, raising complexity to the functional roles of estradiol and testosterone. Readers will find key information about the role of sex hormones in mitochondrial physiology and their relation with aging, apoptosis, and sarcopenia. Chapters integrate important points with the latest information on the subject, including work of leading researchers studying this issue. The book encompasses both structural and functional aspects of the androgen receptor, AR, as well as its clinical implications.

Membrane Androgen Receptor-induced Oxidative Stress

Sex Hormones in Neurodegenerative Processes and Diseases

Epigenetic Cancer Therapy unites issues central to a translational audience actively seeking to understand the topic. It is ideal for cancer specialists, including oncologists and clinicians, but also provides valuable information for researchers, academics, students, governments, and decision makers in the healthcare sector. The text covers the basic background of the epigenome, aberrant epigenetics, and its potential as a target for cancer therapy, and includes individual chapters on the state of epigenome knowledge in specific cancers (including lung, breast, prostate, liver). The book encompasses both large-scale intergovernmental initiatives as well as recent findings across cancer stem cells, rational drug design, clinical trials, and chemopreventative strategies. As a whole, the work articulates and raises the profile of epigenetics as a therapeutic option in the future management of cancer. Concisely summarizes the therapeutic implications of recent, large-scale epigenome studies, including the cancer epigenome atlas Disease targets for pan-specific versus pan-specific inhibitors, a rational drug design approach to epigenetics relevant to pharmacopopgenic clinical applications. Covers new findings in the interplay between cancer stem cells (CSCs) and drug resistance, demonstrating that epigenetic machinery is a candidate target for eradication of these CSCs.

Androgens and the Aging Male
The mechanisms of action of Androgens

A decade ago, oestrogen-containing hormone therapy was viewed as a promising strategy for the prevention and treatment of dementia and age-related cognitive decline. However, treatment trials in women with Alzheimer's disease showed that oestrogens did not reverse cognitive impairment, and clinical trials in healthy older women indicated that oestrogens did not prevent cognitive decline. The Women's Health Initiative Memory Study trial even suggested an increased risk of dementia with treatment in older life. What happened? How are we to understand these findings? What are the implications for middle-aged and older women? What about testosterone, and what about men? And where do we go from here? This book brings together world-renowned experts in basic and clinical research on sex steroids, aging, and cognition to integrate existing findings with emerging new data, and offer challenging hypotheses on these key issues.

Epigenetic Cancer Therapy

Androgen Receptors are the most comprehensive and up-to-date volume on the topic, including discussions of the basic mechanisms of androgen-androgen receptor actions, their roles in the androgen-related diseases, and their potential clinical applications. Key topics covered include: - The discovery and cloning of the androgen receptor; - Androgen receptor coregulators; - Androgen-related genes and their consensus DNA response elements; - Basic mechanism of action including functional analyses, cellular localization and phosphorylation studies; - Cross-talk to other signal transduction systems; - The recent connections of androgens to women's diseases, such as osteoporosis and ovarian cancer. This book is of interest to students, basic scientists, and clinicians as both a study guide and reference of research in the androgen field. It could also be used as an advanced level text in endocrinology, urology, OB/GYN, or oncology.

Understanding Differences and Disorders of Sex Development (DSD)

Androgen Receptors

This textbook contains the latest advances and scientific knowledge from the leading experts in hair biology, hair disorders, and clinical trichology. The book consists of ten sections in which hair biology, hair genetics, hair diagnostics, hair loss types, pathogenesis, treatment options, and restoration techniques are discussed. This book also emphasizes on various genetic and nongenetic alopecia types, differential diagnosis, and the measurement of hair loss. One chapter of the book is devoted to natural products for hair care and treatment. We believe that this textbook will serve as a comprehensive guide to many physicians dealing with hair disorders in their clinical practice.

Steroids

A nuclear receptor (AR), a member of the nuclear receptor superfamily, is a critical mediator of androgenic signaling. Deficiencies in either receptor concentration and/or functional domains of the receptor lead to androgen insensitivity syndrome, indicating that a normal level and function of AR protein is critical. Previous data suggested that ligand-induced up-regulation of cellular AR content represents a critical step in androgen action. To further test this hypothesis, several factors including sex, androgen dosage, and type of ligand were assessed for their effects on the expression of AR in mouse brain through quantitative ICC and western blot. To explore the relationship between androgen induced changes in AR and AR mRNA, a ribonuclease protection assay (RPA), combined with western blot, was employed to measure the time-course changes of these molecules after T treatment. It was demonstrated that gonadectomy (GDX), which removes virtually all endogenous androgens, caused a significant loss of AR. Replacement with testosterone (T) or dihydrotestosterone (DHT) restored AR back to or above that seen in intact animals. The extent of increase in AR correlated linearly to the androgen dose. This regulatory pattern was seen in both male and females. Moreover, the extent of AR up-regulation by different ligands appeared to reflect their relative hormonal potencies. DHT, which is a more potent androgen than T based on its higher affinity for AR, had a longer effect on receptor augmentation compared to T pure AR antagonist, flutamide. Flutamide showed little effect on AR concentration when administered alone to GDX mice. It inhibited agonist induced AR augmentation when injected concurrently with T or DHT at a dose ratio of 100 to 1. In these experiments, a positive correlation between physiological function and the ability of a ligand to upregulate AR was demonstrated. Interestingly, both T and flutamide significantly increased nuclear AR signal, suggesting that the requirement of ligand binding for nuclear translocation of AR is not agonist specific. Finally, down-regulation of steady state AR mRNA content by T was observed following a period of RPA. There appears to be a critical time period when T inhibits AR mRNA and AR protein induced by T, indicating that androgen induced up-regulation of AR is independent of changes in AR mRNA. The current results support the concept that agonists, augment AR level by increasing AR stability.

Hirsutism

Androgens play a critical role in the development and maintenance of the male reproductive system and affect important physiological processes and pathological conditions, including the homeostasis of the normal prostate and prostate cancer. A nuclear receptor: Methods and Protocols is designed to provide a tool box to study various phases of androgen action, from its entry to the cell to the phenotypic response that the cell mounts, with up-to-date techniques for biochemists, molecular biologists, cell biologists, geneticists, and pathologists. The volume opens with a brief review of the research history on androgen action and prostate carcinogenesis, followed by chapters that cover state-of-the-art methods to determine androgen levels in biological tissues and fluids, experimental procedures to study the various aspects of androgen receptor activity, and methodology to study salient examples of interactions between androgen signaling and other major signaling pathways in cells. Written in the successful Methods in Molecular Biology series format, chapters include introductions to their respective topics, lists of the necessary materials and reagents, step-by-step, readily reproducible protocols, and notes on troubleshooting and avoiding known pitfalls. A nonauthoritative and easily accessible, A nuclear receptor: Methods and Protocols provides a comprehensive overview of, and practical guidance on, the diverse methodologies that are propelling androgen action research forward, both for normal physiology as well as in disease states.

The mechanisms of Androgen Action in Androgenetic Alopecia

The androgen receptor (AR) is required for normal prostate development and the onset and progression of prostate cancer. AR has the modular structure characteristic of steroid hormone receptors, with an NH2-terminal transcriptional activation domain, conserved DNA binding domain, hinge region and carboxyl-terminal ligand binding domain. AR mediates the biological effects of androgens by binding testosterone and dihydrotestosterone with high affinity. A binding ligand in the ligand binding domain stabilizes AR through the NH2- and carboxyl-terminal N/C interaction that increases AR
Androgens and androgen receptors (AR) play critical roles in the development and progression of prostate cancer, the most frequently diagnosed cancer and second leading cause of cancer death in US males. AR is an androgen-dependent DNA-binding transcription factor that regulates the expression of androgen-responsive genes. Identification and characterization of androgen-responsive genes provide insights into the cellular mechanisms of androgen action and may lead to new approaches in diagnosis, prognosis, prevention and/or treatment of prostate cancer. This volume provides critical information from well respected experts in the field. Some of the exciting topics include the new understanding of mechanisms underlying the regulation of androgen-responsive gene expression, and functions of various androgen-responsive genes in biological processes essential in carcinogenesis including cell growth, angiogenesis, and epithelial-to-mesenchyme transition (EMT). Other important aspects addressed are the current and potential clinical applications of knowledge on androgen-responsive gene regulation and function. This book is intended for researchers, scientists, faculty, and advanced graduate students with an interest in androgen action and prostate cancer.

A book on testosterone provides a comprehensive overview of the physiological and pathological roles of steroids, with reference to production and action of gonadal steroids, role of steroid sulfonation, sex specific and steroids-dependent mechanism of hippocampal function, and the hydroxysteroid dehydrogenases for the modulation of tissue glucocorticoid availability. We then covered different aspects of steroid application in clinical environment, such as endocrine function after ovarian transplantation, diagnostic significance of salivary assessment of androgens, drawing of serum steroid hormones in sport analysis, serum steroid hormones and vitamins, membrane bound androgenic action and correlation between salivary and serum cortisol responses after alcohol intake. In response to the need to address novel and valuable information on steroids science and medicine, we sincerely hope that this book will enable readers to comprehend this fast-growing and exciting scientific discipline.

Testosterone

This book is an introductory text in neuroendocrinology for undergraduate students.

Hair and Scalp Disorders

The development, growth and survival of eukaryotic organisms require the proper regulation of tens of thousands of genes. Therefore, a correct temporal and spatial expression of genes is crucial. These expression patterns are controlled by a wide variety of mechanisms, but a major level of gene expression occurs at the transcription initiation process. In this part, the basic mechanisms of eukaryotic gene transcription will be discussed. Contents include: 1) General Introduction, 2) Characterization of the two coactivator interacting surfaces of the androgen receptor and their relative role in transcriptional control, 3) Screening for environmental (anti)androgenic activity, 4) Detection of endocrine disrupting activities in pesticides and polychlorinated biphenyls, and 5) General Discussion / Future Perspectives.

Prostate Cancer

Androgens are critical regulators of prostate differentiation and function, as well as prostate cancer growth and survival. Therefore, androgen ablation is the preferred systemic treatment for disseminated prostate cancer. A novel action is exerted in target tissues via binding the androgen receptor (AR), a nuclear receptor transcription factor. Historically, the gene expression program mediated by the AR has been less well understood. However, recent advances in transcriptional profiling and more traditional single-gene characterization studies have revealed many androgen-regulated genes that are important mediators of androgen action in both normal and malignant prostate tissue. This book focuses on the androgen-regulated gene expression program, and examine how recently identified androgen-regulated genes are likely to contribute to the development and progression of prostate cancer. Recent studies that have attempted to unravel how these genes are deregulated in androgen depletion independent prostate cancer will be included.

Genetics of Human Infertility

Androgens and androgen receptors (AR) play critical roles in the development and progression of prostate cancer, the most frequently diagnosed cancer and second leading cause of cancer death in US males. AR is an androgen-dependent DNA-binding transcription factor that regulates the expression of androgen-responsive genes. Identification and characterization of androgen-responsive genes provide insights into the cellular mechanisms of androgen action and may lead to new approaches in diagnosis, prognosis, prevention and/or treatment of prostate cancer. This volume provides critical information from well respected experts in the field. Some of the exciting topics include the new understanding of mechanisms underlying the regulation of androgen-responsive gene expression, and functions of various androgen-responsive genes in biological processes essential in carcinogenesis including cell growth, angiogenesis, and epithelial-to-mesenchyme transition (EMT). Other important aspects addressed are the current and potential clinical applications of knowledge on androgen-responsive gene regulation and function. This book is intended for researchers, scientists, faculty, and advanced graduate students with an interest in androgen action and prostate cancer.

Medicinal Chemistry of Anticancer Drugs

Medicinal Chemistry of Anticancer Drugs, Second Edition, provides an updated treatment from the point of view of medicinal chemistry and drug design, focusing on the mechanism of action of anticancer drugs from the molecular level, and on the relationship between chemical structure and chemical and biochemical reactivity of anticancer agents. Antitumor chemotherapy is a very active field of research, and a huge amount of information on the topic is generated every year. Cytotoxic chemotherapy is gradually being supplemented by a new generation of drugs that target specific alterations in the surface of cancer cells, and resistance to anticancer drugs continues to be investigated. While these therapies are in their infancy, they hold promise of more effective therapies with fewer side effects. Although many books are available that deal with clinical aspects of cancer chemotherapy, this book provides a sorely needed update from the point of view of medicinal chemistry and drug design. Presents information in a clear and concise way using a large number of figures; Historical background provides insights on how the process of drug discovery in the anticancer field has evolved; Extensive references to primary literature

Testosterone

Receptors and Hormone Action, Volume 1, provides an overview of the state of knowledge in hormone action. This book describes basic methodologies and model systems used in the exploration of the molecular bases of hormone action. The chapters present not only a rather extensive description of hormone receptors and their properties, but also basic aspects of structure and function of chromatin and membranes, the roles of which hormones and their receptors exert their action. The receptors discussed include soluble cytoplasmic and nuclear receptors for steroid hormones and vitamins, membrane bound receptors for protein hormones and biogenic amines, and nuclear receptors for thyroid hormones. Receptor types are also covered in view of the large body of literature accumulated on the various functions of these fascinating but elusive molecules. This book is intended for a broad spectrum of readers, including those who have not yet worked in the field as well as those who have considerable expertise in one or another aspect of hormone action.
Infertility affects more than one in ten couples worldwide and is related to highly heterogeneous pathologies sometimes only discernible in the germ line. Its complex etiology often, but not always, includes genetic factors besides anatomical defects, immunological interference, and environmental aspects. Nearly 30% of infertility cases are probably caused only by genetic defects. Thereby experimental animal knockout models convincingly show that infertility can be caused by single or multiple gene defects. Translating those basic research findings into clinical studies is challenging, leaving genetic causes for the vast majority of infertility patients unexplained. Nevertheless, a large number of candidate genes have been revealed by sophisticated molecular methods. This book provides a comprehensive overview on the subject of infertility written by the leading authorities in this field. It covers topics including basic biological, cytological, and molecular studies, as well as common and uncommon syndromes. It is a must-read for human geneticists, endocrinologists, epidemiologists, zoologists, and counsellors in human genetics, infertility, and assisted reproduction.

A utoregulation of Androgen Receptor by Androgen in Mouse Brain

Prostate cancer is the second leading cause of death in men and its progression is highly dependent on androgens and androgen receptors. However, even with treatment, eventually most prostate cancers progress. Studies of the mechanisms behind this progression leads to advances in treatments for androgen-related diseases.

The Sertoli Cell

The androgen receptor (AR) mediates a wide range of physiological actions of androgens in cells and tissues. Contributions to this volume cover distinct topics of AR signalling, extending from the structural aspects of AR to its role in androgen-associated diseases and potential clinical applications. Some key issues covered include an overview of structural aspects of AR genes and proteins in mammalian and non-mammalian vertebrate species and a description of the identified AR splice variants in pathological and non-pathological conditions. The structural and functional analysis of coding and untranslated regions of AR are discussed in the context of diseases such as androgen insensitivity syndrome, spinal and bulbar muscular atrophy, polycystic ovarian syndrome and breast, ovary and prostate cancers. The role of AR regulated genes implicated in prostate cancer progression is also explored. This book is a comprehensive conceptual review of the recent findings on AR genes and protein structure, molecular variants, ligands, target genes and signalling mechanisms. Graduate students, scientists and professionals can use it as both a study text and a reference for research purposes.

Proceedings of the Fourth International Congress on Hormonal Steroids

Acting principally to control patterns of gene expression, nuclear receptors play vital roles during embryonic development and in the regulation of metabolic and reproductive functions in adult life, which proves this superfamily of ligand-activated transcription factors to be a crucial part of biological life. In The Nuclear Receptor Superfamily: Methods and Protocols, expert researchers describe a range of molecular, structural and cell biological techniques currently used to investigate the structure-function of nuclear receptors, together with experimental approaches that may lead to new therapeutic strategies for treating nuclear receptor-associated diseases. Written in the highly successful Methods in Molecular Biology™ series format, the chapters in this volume contain brief introductions to the topics, lists of the necessary materials and reagents, step-by-step, readily reproducible laboratory protocols, as well as notes from the experts to highlight tips on troubleshooting and avoiding known pitfalls. Cutting-edge and easy to use, The Nuclear Receptor Superfamily: Methods and Protocols provides beneficial and time-saving guidance for all those undertaking research in this ever-growing field of study.