Mouse Models Of Developmental Genetic Disease

#mouse models #developmental genetic disease #genetic disease research #animal models disease #preclinical drug discovery

Mouse models are indispensable tools for understanding the complex mechanisms of developmental genetic diseases. These preclinical animal models provide invaluable insights into disease progression, gene function, and potential therapeutic strategies, enabling researchers to study human genetic disorders in a controlled environment and facilitating the development of novel treatments and interventions.

Mouse Models of Developmental Genetic Disease

Approximately three percent of newborn humans have congenital anomalies with significant cosmetic and/or functional consequences. Much of our ability to understand what has gone awry in these birth defects rests with development of animal models for them; the mouse has emerged as the model organism of choice for these studies. This volume reviews mouse models of specific developmental genetic diseases, including neural tube defects; cleft lip and/or palate; congenital heart disease; ciliopathies; hereditary deafness and others to provide conceptual insight into congenital anomalies generally. The interplay between clinical observation and murine model systems is expected to yield deep insight into mammalian developmental processes and the emergence of effective preventive and/or therapeutic strategies. Provides busy clinical and basic science researchers a one-stop overview and synthesis of the latest research findings and contemporary thought in the area Allows researchers to compare and contrast disease models and also to learn about what models have been developed for large-scale distribution Allows researchers to evaluate basic differences in mouse and human biology and propose alternate pathways and possible gene interactions of the disease

Mouse Models of the Nuclear Envelopathies and Related Diseases

Volume 109 of Current Topics in Developmental Biology covers mouse models of the nuclear envelopathies and related diseases, with contributions from an international board of authors. The chapters provide a comprehensive set of reviews covering such topics as mouse models neurodegenerative diseases including Parkinson’s and dystonia, muscle ageing and sarcopenia, cardiac failure and repair, ageing and prospects lifespan extension, lipodystrophy and the significance in fat regulation, also identifying developmental mutations in mammals and nuclear envelope and LINC complex in disease. Covers the area of mouse models of developmental genetic disease International board of authors Provides a comprehensive set of reviews covering such topics as mouse models neurodegenerative diseases including Parkinson’s, muscle aging, lipodystrophy, and more

Mouse Models in the Study of Genetic Neurological Disorders

The number of mouse models that are available for the study of human genetic neurological disorders is large and growing rapidly. Therefore, it was difficult to select the models that were reviewed in this volume. Clearly, there are important models that are not discussed, and perhaps a volume twice this size would have been more appropriate. Moreover, the pace at which new models are being developed and analyzed is rapid. As this volume goes to press, I am sure that additional mouse genes responsible for naturally occurring neurological disorders are being discovered and that many new transgenic and mutant mouse strains are being developed. Therefore, this volume should not be viewed as a comprehensive compendium, but rather as an update of work in progress. It is exhilarating to witness the fast pace at which these models are being established as important tools in the study of basic neuroscience and neurological disorders. It will be even more exciting to see their utilization in the development and testing of therapeutic interventions for these diseases. I would like to thank each of the authors who have contributed to this volume for their time and their expertise. I would also like to thank Drs. Timothy Coetzee and Joshua Corbin for their advice in the selection of the topics covered. I am deeply indebted to Dr. Kunihiko Suzuki, who first approached me with the idea for this volume, for his guidance throughout its preparation.

Mouse Models of Development and Disease

Mouse Models of Development and Disease, Volume 148 in the Current Topics in Developmental Biology series, highlights new advances in the field, with this volume presenting chapters describing Mouse models of Charcot-Marie-Tooth disease, Mouse models in palate and craniofacial development, Uterine morphogenesis, Improving the translatability of mouse models of Alzheimer's disease, Mouse models for the study of clustered protocadherins, Mechanisms of organ regeneration in the spiny mouse, Comparative studies of organ vascularization, Modeling human urinary tract development and hereditary malformations, Innervation in organogenesis, Between embryo and adult: somatic growth of the kidney, and Mouse models in the study of Notch signaling. Provides the authority and expertise of leading contributors from an international board of authors Presents the latest release in the Current Topics in Developmental Biology series Updated release includes the latest information on Mouse Models of Development and Disease

Mouse Models of Human Cancer

Mice have become the species of choice for modeling the complex interactions between tumor cells and the host environment. Mouse genetics are easily manipulated, and a growing array of technology exists for this purpose. Mouse models allow investigators to better understand causal relationships between specific genetic alterations and tumors, utilize new imaging techniques, and test novel therapies. Recent developments along these lines show great promise for the development of new anti-cancer treatments. Mouse Models of Human Cancer provides researchers and students with a complete resource on the subject, systematically presenting the principles, methodologies, applications, and challenges associated with this exciting field. Offering a survey of the latest research and a description of future areas of interest, this text: Presents real experimental data Describes organ site-specific mouse models Clearly identifies suitable models for further drug testing Critically analyzes current methodologies and their limitations Features numerous recognizable expert contributors Lists key Web sites, reagents, and companies From mouse handling and genetic engineering to preclinical trials, Mouse Models of Human Cancer is a comprehensive guide to using these models and relating them to human disease. Its uniform presentation describes organ-specific models in clinical, imaging, and

molecular terms, and lays out the relevant genetics, experimental approaches, histological comparisons with human disease, and conclusions. Combining stellar chapter authors, rich illustrations, and clear, up-to-date coverage, Mouse Models of Human Cancer is an invaluable resource for advanced students and cutting-edge researchers.

Mouse Models of Human Blood Cancers

In this book, Dr. Li and his author team plan to emphasize why mouse models are useful in vivo systems for understanding disease mechanisms and developing therapeutic strategies in blood cancers. The authors do not intend to cover all types of blood cancers; instead, they will focus on some major ones such as leukemias and lymphomas. However, the authors will try to cover as much as they can the cancer types and point out that many blood cancers need to be studied in mouse disease models although they are still not available at present. A major focus in the book will be to show what we can or cannot learn from mouse disease models and to also show the critical contributions of mouse models in therapeutic drug development.

Principles of Developmental Genetics

Unlike anything currently available in the market, Dr. Sally A. Moody and a team of world-renowned experts provide a groundbreaking view of developmental genetics that will influence scientific approaches in embryology, comparative biology, as well as the newly emerging fields of stem cell biology and regenerative medicine. Principles of Developmental Genetics highlights the intersection of developmental biology with new revolutionary genomic technologies, and details how these advances have accelerated our understanding of the molecular genetic processes that regulates development. This definitive resource provides researchers with the opportunity to gain important insights into the clinical applicability of emerging new technologies and animal model data. This book is a must-have for all researchers in genetics, developmental biology, regenerative medicine, and stem cell biology. • Includes new research not previously published in any other book on the molecular genetic processes that regulates development • Chapters present a broad understanding on the application of animal model systems, allowing researchers to better treat clinical disorders and comprehend human development • Relates the application of new technologies to the manipulation of stem cells, causes of human birth defects, and several human disease conditions • Each chapter includes a bulleted summary highlighting clinical aspects of animal models

Genetically Engineered Mice Handbook

While mice have always been highly popular laboratory subjects, their suitability for genetic engineering has solidified their position as today's lab animal model of choice. However, their increased use in genetic studies has created a demand for input on phenotyping that is not always easily met. To improve the flow of information on the pathology of mice with spontaneous or genetically engineered mutations, prominent researchers organized a series of meetings. Recognizing other needs, the organizers gradually broadened their focus, until finally they expanded to provide an overview of the entire field of genetically engineered models. The Genetically Engineered Mice Handbook is an extension of those meetings. It offers an introduction for those entering into this area of research, while also serving as a resource for those presently employing mice as laboratory models. Highly comprehensive, this volume covers pertinent aspects of genetically engineered mice, including the use of models for developmental biology and the monitoring of laboratory colonies. With contributions from nearly five-dozen leading researchers, the text presents systematic approaches for analyzing mutant mice for specific medical applications, details a variety of methods for creating mutants and includes information that is particularly hard to access dealing with legal responsibilities. This essential reference examines commonly used traditional, as well as emerging, technologies To address the purpose of the original meeting, the Genetically Engineered Mice Handbook directs researchers to the best public websites, and offers instruction on how to use them. In the past, as their work dictated, researchers would seek out experts on particular organ systems. Now groups of experts work together to generate these websites, providing the latest data as well as discussions over points of debate. These sites do not eliminate the need for a trained pathologist, but they do provide reference materials for those lacking expertise in particular anatomic structures. They also offer much greater numbers of examples than are available in print, from which biomedical researchers can draw.

Genetically Engineered Mice for Cancer Research

Genetically-engineered mouse models for cancer research have become invaluable tools for studying cancer biology and evaluating novel therapeutic approaches. This volume focuses on state-of-the-art methods for generating, analyzing and validating such models for studying aspects of human cancer biology. Additionally, these models are emerging as important pre-clinical systems in which to test cancer prevention and therapeutic strategies in order to select compounds for testing in clinical trials.

Animal Models of Behavior Genetics

This stimulating analysis reviews the broad potential of animal models to foster a deeper understanding of human pathology, strengthen connections between genetic and behavioral studies, and develop more effective treatments for mental disorders. Widely-studied and lesser-used species are examined in models that capture features along the continuum of normative and pathological behavior. The models highlight genetic causes of core features, or endophenotypes, of developmental, internalizing, and externalizing disorders, as well as dementia. Expert contributors address questions ranging from how suitable species are chosen for study to the costs and benefits of using inbred versus outbred strains, and the effects of housing environment on subject animals. Larger issues addressed include how to evaluate the applicability of animal behavioral models to the human condition and how these models can harness emerging molecular technologies to further our understanding of the genetic basis of mental illness. Included in the coverage: Mating and fighting in Drosophila. Attachment and social bonding. Impulsivity in rodents and humans. Animal models of cognitive decline. Animal models of social cognition. Future directions for animal models in behavioral genetics. A detailed map of where this evolving field is headed, Animal Models of Behavior Genetics shows geneticists, molecular biologists, and cognitive neuroscientists paths beyond established concepts toward a more knowledgeable and collaborative future.

Mouse Models for Drug Discovery: Methods and Protocols

With genetic engineering, systems explored in this book now exist allowing for the simple, efficient, and near universally precise genetic manipulation directly in any organism, including the mouse. Herein, these models are applied to a wide field of disease areas, including diabetes, cardiovascular disease, skin disorders, cancer, neurodegenerative and neuromuscular diseases, retinal disorders, as well as various behavioral models. Written for the highly successful Methods in Molecular Biology series, chapters include introductions to their respective topics, lists of the necessary materials and reagents, step-by-step, readily reproducible laboratory protocols, and tips on troubleshooting and avoiding known pitfalls. Practical and fully updated, Mouse Models for Drug Discovery: Methods and Protocols, Second Edition serves to equip the reader with an extensive overview of techniques to utilize the many possibilities of mice in the drug development process.

Inborn Errors of Development

In this book, the clinical chapters are organized into sections by defined developmental pathways or gene families, and each section is preceded by a general overview. For each disorder the authors cover the disease-causing genes, the role of these genes in development as elucidated in model organisms, the human mutations that have been identified, and the developmental pathogenesis of the condition. Clinical descriptions, along with discussions of therapy and counseling, are provided. This book will be an invaluable resource for physicians, dentists, and other health professionals and for basic scientists interested in developmental processes and genetic perturbations that affect them.

The Genetics of Neurodevelopmental Disorders

Neurodevelopmental disorders arise from disturbances to various processes of brain development, which can manifest in diverse ways. They encompass many rare genetic syndromes as well as common, heritable conditions such as intellectual disability, autism, ADHD, schizophrenia and many types of epilepsy. The Genetics of Neurodevelopmental Disorders examines recent revolutionary advances in our understanding of the genetics of these disorders, exploring both basic discoveries and the translation of new findings into the clinical setting. The book begins by examining the genetic architecture and etiology of neurodevelopmental disorders. It describes the striking recent progress in identifying pathogenic mutations, which are grouped here based on the neurodevelopmental processes impacted. Subsequent chapters consider the use of cellular and animal models to elucidate the cascading consequences of such mutations, from molecular and cellular levels to emergent effects on neural circuits, brain systems and subsequent psychological development. The text concludes by

examining the important clinical implications of the recent advances in the field, from recognition of the genetic causes in individual patients to development of new treatments and interventions. A timely synthesis, The Genetics of Neurodevelopmental Disorders is a unique and essential resource for neuroscientists, geneticists, neurologists and psychiatrists and an accessible and up-to-date overview for medical and science students.

Development of Humanized Mouse Models for Infectious Diseases and Cancer

Bringing together top-level contributions on all aspects of the subject, this book provides an overview of the recent advances in the genetics of respiratory control in health and disease. It also shows how combined studies in humans and mouse models have helped to improve our understanding of the mechanisms that underlie genetically determined respiratory control disorders with the goal of developing new therapeutic interventions.

Genetic Basis for Respiratory Control Disorders

Marten Hofker and Jan van Deursen have assembled a multidisciplinary collection of readily reproducible methods for working with mice, and particularlyfor generating mouse models that will enable us to better understand gene function. Described in step-by-step detail by highly experienced investigators, these proven techniques include new methods for conditional, induced knockout, and transgenic mice, as well as for working with mice in such important research areas as immunology, cancer, and atherosclerosis. Such alternative strategies as random mutagenesis and viral gene transduction for studying gene function in the mouse are also presented.

Transgenic Mouse Methods and Protocols

Introduction.-Probing Astrocyte Function in Fragile X Syndrome.- Neural Stem Cells.- Fragile X Mental Retardation Protein (FMRP) and the Spinal Sensory System.– The Role of the Postsynaptic Density in the Pathology of the Fragile X Syndrome.- Behavior in a Drosophila model of Fragile X.- Molecular and Genetic Analysis of the Drosophila Model of Fragile X Syndrome.- Fragile X Mental Retardation Protein and Stem Cells.- Manipulating the Fragile X Mental Retardation Proteins in the Frog.- Exploring the Zebra finch Taeniopygia gutta as a Novel Animal Model for the Speech-language Deficit of Fragile X Syndrome.- Neuroendocrine Alterations in the Fragile X Mouse.- Taking STEPs forward to understanding Fragile X Syndrome.- Fmr-1 as an Offspring Genetic and a Maternal Environmental Factor in Neurodevelopmental Disease.- Mouse Models of the Fragile X Premutation and the Fragile X Associated Tremor/Ataxia Syndrome.- Clinical Aspects of the Fragile X Syndrome.- Fragile X Syndrome: A Psychiatric Perspective.- Fragile X Syndrome and Targeted Treatment Trials.- The Fragile X-associate Tremor Ataxia Syndrome.- Vignettes: Models in Absentia.

Modeling Fragile X Syndrome

This fully updated edition provides selected mouse genetic techniques and their application in modeling varieties of human diseases. The chapters are mainly focused on the generation of different transgenic mice to accomplish the manipulation of genes of interest, tracing cell lineages, and modeling human diseases. Written for the highly successful Methods in Molecular Biology series, chapters include introductions to their respective topics, lists of the necessary materials and reagents, step-by-step, readily reproducible laboratory protocols, and tips on troubleshooting and avoiding known pitfalls. Authoritative and up-to-date, Mouse Genetics: Methods and Protocols, Second Edition delivers fundamental techniques and protocols to geneticists, molecular biologists, cell and developmental biologists, students, and postdoctoral fellows working in the various disciplines of genetics, developmental biology, mouse genetics, and modeling human diseases.

Mouse Genetics

This book describes human development including sexual reproduction and stem cell research with the development of model organisms that are accessible to genetic and experimental analysis in readily understandable texts and 315 multi-colored graphics. The introductory account of model organisms selected from the entire animal kingdom presents general principles, which are then outlined in subsequent chapters devoted to, for example, sexual development; genes controlling development and their contemporary molecular-analysis methods; production of clones and transgenic animals; development of the nervous and circulatory systems; regenerative medicine and ageing. Finally the

evolution of developmental toolkits and novelties is discussed including the genetic basis of the enlargement of the human forebrain. Separate boxes are devoted to controversial questions such as the benefits and problems of prenatal diagnostics or the construction of ancient body plans.

Development and Reproduction in Humans and Animal Model Species

This book focuses on the use of animal models to study various human defects. It summarizes our current understanding of a variety of common human birth defects and the essential role of animal models in shedding light on the underlying mechanisms of these disorders. Birth defects are the leading cause of infant deaths, and cost billions of dollars in care for those affected. Unfortunately, the lack of a clear understanding of the mechanisms leading to many of these developmental disorders has hindered effective prevention and early intervention strategies. Studies using animal models have provided essential insights into several human birth defects. This book serves as a valuable reference resource for researchers and graduate students who are interested in learning the basic principles as well as the latest advances in the study of the mechanisms of human birth defects.

Animal Models of Human Birth Defects

Animal models of diseases play a pivotal role in drug discovery and development, not only for proof of the concept studies of efficacy, PK/PD relationship but also for drug safety assessment. Since considerable differences in variables exist between animal models and human models (such as genetics, physiology, anatomy, gene expression, heterogeneity of disease conditions, etc.), not all the preclinical models are able to represent the pathophysiological conditions in human diseases. Therefore, partly due to the lack of congruency between animal and human disease models, several proposed therapeutic agents in the past decades have been demonstrated to be effective in preclinical models but failed in clinical studies. This e-book focuses on animal models of diseases from a translational perspective and highlights the key advantages and limitations of each model described to facilitate drug discovery and development. A unique feature of the volume is that it contains a selection of details disease models in various therapeutic niches with significant unmet medical needs, including inflammation, neurological diseases, cardiovascular and metabolic diseases, and oncology. This e-book is, therefore, of considerable value to researchers and clinicians involved in drug discovery and development as well as pathology.

Translational Animal Models in Drug Discovery and Development

Published in 2005: Genetics of Developmental Disabilities is written as a textbook and resource for physicians, basic and clinical researchers, and other professionals, students, and health care providers. Those interested in the causes and scientific understanding of developmental disabilities.

Genetics of Developmental Disabilities

Animal Models for the Study of Human Disease identifies important animal models and assesses the advantages and disadvantages of each model for the study of human disease. The first section addresses how to locate resources, animal alternatives, animal ethics and related issues, much needed information for researchers across the biological sciences and biomedicine.The next sections of the work offers models for disease-oriented topics, including cardiac and pulmonary diseases, aging, infectious diseases, obesity, diabetes, neurological diseases, joint diseases, visual disorders, cancer, hypertension, genetic diseases, and diseases of abuse. Organized by disease orientation for ease of searchability Provides information on locating resources, animal alternatives and animal ethics Covers a broad range of animal models used in research for human disease

Animal Models for the Study of Human Disease

The costs associated with a drug’s clinical trials are so significant that it has become necessary to validate both its safety and efficacy in animal models prior to the continued study of the drug in humans. Featuring contributions from distinguished researchers in the field of cognitive therapy research, Animal Models of Cognitive Impairment examines some of the most popular and successful animal archetypes used in the context of drug discovery. It provides integrated coverage of the latest research concerning neuronal systems relevant to cognitive function and dysfunction, assimilating reviews of this research within the context of each chapter. This approach is unique in that it brings together molecular and neurochemical methodologies, behavioral applications in translational models,

and clinical applications. The book comprehensively discusses a wide variety of animal models of cognitive impairment, including genetic, lesion, pharmacological, and aging related impairments. It also explores the significance of this research in regards to the treatment of various addictions and disorders such as stroke, autism, Alzheimer's, schizophrenia, and ADHD. Edited by two renowned authorities in the field, Animal Models of Cognitive Impairment is a timely book that provides integrated coverage of cutting-edge research that concerns neuronal systems relevant to cognitive function and dysfunction.

Animal Models of Cognitive Impairment

Fragile X Syndrome: From Genetics to Targeted Treatment provides a structured overview of the molecular and clinical background of the disorder as well as treatment options. The book discusses the detailed molecular information on each of the pathways involved with sufficient details for all whose research touches this pathway. It provides a state-of-the-art update on all clinical aspects associated with this syndrome, including phenotype, diagnostics and epidemiology. It also includes an overview of the lessons learned from the preclinical research and pioneering trials on the fragile X syndrome for the investigators involved in clinical trials of neurodevelopmental disorders. This book is written for academic researchers, pharmaceutical investigators, and clinicians in the field who work on the disorder, and for researchers involved in clinical trials of the fragile X syndrome or related disorders. Provides a comprehensive overview of the molecular genetics, clinical trials, and treatment of Fragile X Syndrome Written for academic researchers, pharmaceutical investigators, and clinicians in the field Edited by international leaders in the field who have contributed greatly to the study of Fragile X Syndrome Directs the reader through complex issues surrounding FXS and draws the literature together for researchers and clinicians

Fragile X Syndrome

Genetics of Bone Biology and Skeletal Disease, Second Edition, is aimed at students of bone biology and genetics and includes general introductory chapters on bone biology and genetics. More specific disease orientated chapters comprehensively summarize the clinical, genetic, molecular, animal model, molecular pathology, diagnostic, counseling, and treatment aspects of each disorder. The book is organized into five sections that each emphasize a particular theme, general background to bone biology, general background to genetics and epigenetics, disorders of bone and joint, parathyroid and related disorders, and vitamin D and renal disorders. The first section is specifically devoted to providing an overview of bone biology and structure, joint and cartilage biology, principles of endocrine regulation of bone, and the role of neuronal regulation and energy homeostasis. The second section reviews the principles and progress of medical genetics and epigenetics related to bone disease, including genome-wide association studies (GWAS), genomic profiling, copy number variation, prospects of gene therapy, pharmacogenomics, genetic testing and counseling, as well as the generation and utilizing of mouse models. The third section details advances in the genetics and molecular biology of bone and joint diseases, both monogenic and polygenic, as well as skeletal dysplasias, and rarer bone disorders. The fourth section highlights the central role of the parathyroids in calcium and skeletal homeostasis by reviewing the molecular genetics of: hyperparathyroidism, hypoparathyrodism, endocrine neoplasias, and disorders of the PTH and calcium-sensing receptors. The fifth section details molecular and cellular advances across associated renal disorders such as vitamin D and rickets. Identifies and analyzes the genetic basis of bone disorders in humans and demonstrates the utility of mouse models in furthering the knowledge of mechanisms and evaluation of treatments Demonstrates how the interactions between bone and joint biology, physiology, and genetics have greatly enhanced the understanding of normal bone function as well as the molecular pathogenesis of metabolic bone disorders Summarizes the clinical, genetic, molecular, animal model, molecular pathology, diagnostic, counseling, and treatment aspects of each disorder

Genetics of Bone Biology and Skeletal Disease

This book provides up-to-date information on the use of transgenic mouse models in the study of neurodegenerative disorders. The editors have extensive knowledge and experience in this field and the book is aimed at undergraduates, postgraduates and academics.

Animal Models for Neurodegenerative Disease

Following the completion of the mouse and human genome sequences, a major challengeisthefunctionalcharacterizationofeverymammaliangeneandthedeciph- ing of their molecular interaction network.

The mouse offers many advantages for the use of genetics to study human biology and disease, unmatched among other m- mals. Its development, body plan, physiology, behavior, and diseases have much in common, based on the fact that 99% of the human genes have a mouse ortholog. The investigation of gene function using mouse models is based on many years of tech- logical development. In the two decades since gene targeting in murine embryonic stem (ES) cells was first described by Mario Capecchi and colleagues, more than 3000 predesigned mouse mutants have been developed. To date, a variety of mouse mutagenesis techniques, either gene- or phenotype-driven, are used as systematic approaches. The availability of the genome sequence supports gene-driven approaches such as gene-trap and targeted mutagenesis in ES cells, allowing efficient and precise gene disruption. In combination with the use of site-specific DNA recombinases, in particular the Cre/loxP system, gene disruptioncan be directed to specific cell types in conditionalmousemutants. Furthermore,chemicalandtransposonmutagenesisofthe mouse genome enables us to perform phe- notype-driven screens for the unbiased identification of phenotype–genotype correlations involved in models of human d- ease. Over the next several years, the mouse genome will be systematically altered, and the techniques for achieving predesigned manipulations will be constantly developed further and improved. The second edition of Gene Knockout Protocols brings together distinguished c- tributorswithextensiveexperienceinthegenetargetingandmousegeneticsfields.

Gene Knockout Protocols

Ultimately, the quality of the tools available for genetic analysis and experimental disease models will be assessed on the basis of whether they provide new information that generates novel treatments for human disease. In addition, the time frame in which genetic discoveries impact clinical practice is also an important dimension of how society assesses the results of the significant public financial investment in genetic research. Because of the investment and the increased expectation that new tre- ments will be found for common diseases, allowing decades to pass before basic discoveries are made and translated into new therapies is no longer acceptable. Computational Genetics and Genomics: Tools for Understanding Disease provides an overview and assessment of currently available and developing tools for genetic analysis. It is hoped that these new tools can be used to identify the genetic basis for susceptibility to disease. Although this very broad topic is addressed in many other books and journal articles, Computational Genetics and Genomics: Tools for Understanding Disease focuses on methods used for analyzing mouse genetic models of biomedically - portant traits. This volume aims to demonstrate that commonly used inbred mouse strains can be used to model virtually all human disea- related traits. Importantly, recently developed computational tools will enable the genetic basis for differences in disease-related traits to be rapidly identified using these inbred mouse strains. On average, a decade is required to carry out the development process required to demonstrate that a new disease treatment is beneficial.

Computational Genetics and Genomics

Prostate carcinogenesis is a multi-step process resulting in the transformation of prostatic epithelial cells into invasive carcinoma and metastasis. In recent years, mouse models have emerged that recapitulate salient features of prostate carcinogenesis found in human disease. These models illu- minate the molecular events that result in transformation and disease progression. In addition, mouse models can be used to identify molecular targets and test chemotherapeutic agents that may alter the course of disease. We have generated a new mouse model to further delineate targets that may halt cancer progression and lead to regression of disease. Crossing the TRAMP mouse with the PSCA-TVA transgenic mouse has resulted in the TRAMP-TVA mouse that is destined to develop prostate cancer and expresses the avian viral receptor, TVA, on prostate cancer cells. This new transgenic mouse should enable specific gene transfer of imaging genes and small hairpin nuclear RNAs (shRNAs) resulting in knockdown of specific targets. TRAMP-TVA mice demonstrate PIN lesions at 8 weeks and develop adenocarcinoma at 6-15 months. We have been able to demonstrate PSCA-driven expression of the TVA viral receptor in these lesions. Intraperitoneal injection of virus containing the luciferase gene results in luminescence signal in the prostate. Further development of this model will enable the effect of target gene knockdown via RNA interference to be monitored non-invasively in mice. This approach will facilitate high throughput analysis of potential shRNA targets.ta.

Development of a Mouse Model for Prostate Cancer Imaging and Study of Disease Progression

The laboratory mouse is an important model for addressing questions in cancer biology. In recent years, the questions have become more refined, and mouse models are increasingly being used to develop and test cancer therapeutics. Thus, the need for more sophisticated and clinically relevant mouse models has grown, as has the need for innovative tools to analyze and validate them. This laboratory manual provides cutting-edge methods for generating and characterizing mouse models that accurately recapitulate many features of human cancer. The contributors describe strategies for producing genetic models, including transgenic germline models, gene knockouts and knock-ins, and conditional and inducible systems, as well as models derived using transposon-based insertional mutagenesis, RNA interference, viral-mediated gene delivery, and chemical carcinogens. Tissue recombination, organ reconstitution, and transplantation methods to develop chimeric, allograft, and xenograft models are covered. Approaches to characterize tumor development, progression, and metastasis in these models using state-of-the-art imaging and histopathological, surgical, and other techniques are also included. Other chapters cover the use of mouse models to test and optimize drugs in pre-, co-, and postclinical trials. An appendix specifically addresses the use of mouse cancer models in translational studies and the integration of mouse and human clinical investigations. This manual is therefore an indispensable laboratory resource for all researchers, from the graduate level upward, who study cancer and its treatment.

Mouse Models of Cancer

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.

Genetics of Human Infertility

The availability of well-defined genetic strains and the ability to create transgenic and knockout mice makes mouse models extremely valuable biomedical tools. Their suitability as an experimental system for cardiovascular research depends on the individual investigator's ability to manipulate the mice surgically. Many mouse models require microsurgical techniques, which hitherto could not be performed without practical training. This comprehensive handbook will enable scientists to develop these models in their own laboratories. It contains detailed advice on the issues that investigators need to consider before starting their experiments. It then provides essential information about experimental procedures, specific instruments and technical knowledge and will prove an indispensable guide to all scientists planning to work with these mouse models. This book includes a brief introduction to each disease, followed by a detailed description of the methods and materials used to establish the relevant mouse model. Each chapter has been written by an expert familiar with that system, who provides helpful discussion of the problems that may be encountered and examples of applications of the model. Importantly, each technique is clearly illustrated on the accompanying CD, so that researchers can observe the operational procedures directly. With coverage of all the major mouse models of cardiovascular disease, this book may be used to obtain a broad overview of commonly used methods and, more importantly, as a comprehensive source of detailed information on the development and study of such models. It will prove essential reading to all those working on experimental animal models of cardiovascular disease, from students to independent investigators.

A Handbook of Mouse Models of Cardiovascular Disease

Genetic Models and Molecular Pathways Underlying Autism Spectrum Disorders, Volume 241 provides the most recent information on the animal model systems that are available to study different forms of autism spectrum disorders. In addition to genetically engineered animals that uniquely model genetic forms of ASD, this volume also provides detailed chapters on a variety of specific topics, including An

overview of genetic models of ASDs, Phenotypic modeling of ASD symptoms, Molecular mechanisms of NF1 model of ASD symptoms, Ube3a gene dosage disorders: molecular and circuit mechanisms of ASD, Circuit dysfunctions in ASD models, ERK signaling in genetic models of ASD, and more. Presents a timely, comprehensive assessment of the field Includes helpful summaries on current knowledge, gaps and future directions in autism research

Genetic Models and Molecular Pathways Underlying Autism Spectrum Disorders

Precision medicine is focused on the individual and will require the rapid and accurate identification and prioritization of causative factors of disease. To move forward and accelerate the delivery of the anticipated benefits of precision medicine, developing predictable, reproducible, and reliable animal models will be essential. In order to explore the topic of animal-based research and its relevance to precision medicine, the National Academies of Sciences, Engineering, and Medicine convened a 2-day workshop on October 5 and 6, 2017. The workshop was designed to focus on the development, implementation, and interpretation of model organisms to advance and accelerate the field of precision medicine. Participants examined the extent to which next-generation animal models, designed using patient data and phenotyping platforms targeted to reveal and inform disease mechanisms, will be essential to the successful implementation of precision medicine. This publication summarizes the presentations and discussions from the workshop.

Advancing Disease Modeling in Animal-Based Research in Support of Precision Medicine

This is the first book to assemble the leading researchers in the field of LRRK2 biology and neurology and provide a snapshot of the current state of knowledge, encompassing all major aspects of its function and dysfunction. The contributors are experts in cell biology and physiology, neurobiology, and medicinal chemistry, bringing a multidisciplinary perspective on the gene and its role in disease. The book covers the identification of LRRK2 as a major contributor to the pathogenesis of Parkinson's Disease. It also discusses the current state of the field after a decade of research, putative normal physiological roles of LRRK2, and the various pathways that have been identified in the search for the mechanism(s) of its induction of neurodegeneration.

Leucine-Rich Repeat Kinase 2 (LRRK2)

One of the Most Rapidly Advancing Fields in Modern Neuroscience The success of molecular biology and the new tools derived from molecular genetics have revolutionized pain research and its translation to therapeutic effectiveness. Bringing together recent advances in modern neuroscience regarding genetic studies in mice and humans and the practicality of clinical trials, Translational Pain Research: From Mouse to Man effectively bridges the gap between basic research and patient care by humanely examining rodent models for pain associated with bone cancer, osteoarthritis, fibromyalgia, and cardiac episodes. Distinguished Team of International Contributors In addition to addressing the groundbreaking technical advances in tract tracing, endocannabinoids, cannabis, gene therapy, siRNA gene studies, and the role of glia, cytokines, P2X receptors and ATP, this book also presents cutting-edge information on: Nociceptor sensitization Muscle nociceptors and metabolite detection Visceral afferents in disease Innovative rodent model for bone cancer pain Highly specific receptor cloning Modular molecular mechanisms relevant to painful neuropathies This sharply focused work also discusses unexpected discoveries derived from brain-imaging studies related to thalamic pain. Translational Pain Research covers the progress made toward bringing laboratory science (much of it at the molecular level) to our understanding of pain phenomena in humans, with the ultimate goal of reducing the suffering that often accompanies pain and its indirect consequences.

Translational Pain Research

Atlas of Epilepsies is a landmark, all-encompassing, illustrated reference work and hands-on guide to the diagnosis, management and treatment of epilepsy in all its forms and across all age groups. The premier text in the field with over one thousand images, the Atlas’s highly illustrative approach tackles the difficult subject of epileptic seizures and epileptic syndromes, accompanied by sequential photographs of each management step. Intraoperative photographs are accompanied by detailed figure legends describing nuances, subtleties, and the thought processes involved in each step, providing a fuller understanding of each procedure. The Atlas draws on the expertise of over 300 internationally-renowned experts, and is liberally interspersed with clinical insights and personal vignettes that offer helpful tips, technical advice and critical knowledge to the clinician and scholar. The thorough

and complete table of contents includes dedicated sections or chapters on important topics such as neonatal and pediatric seizures; imitators of epilepsy; EEG and neuroimaging; psychiatric and quality of life aspects of epilepsy; and a complete guide to treatment options including current and up-to-date chapters on pharmaceuticals, surgical procedures, and additional and alternative treatments. No other publication addresses epilepsies as thoroughly and completely as the Atlas of Epilepsies. Exhaustive and illustrative, convenient and current, this reference is sure to be the premier text on epilepsy for many years to come.

Atlas of Epilepsies

Origins of Inbred Mice documents the proceedings of a symposium on the state of knowledge on inbred mice held in Bethesda, Maryland, in 1978. The book is organized into seven parts. Part I provides introductory remarks on the history of the development of inbred mice. Part II contains papers that examine mutations of inbred strains of mice. Part III contains studies dealing with viruses that affect inbred mice, including those that cause leukemia and mammary tumors. Part IV examines histocompatibility genes and their antigens; cell surface antigens of mouse leukemia; the characteristics of genes of the Tla region of the mouse; and the use of recombinant inbred strains in gene mapping. Part V presents studies on differences among sublines of inbred mouse strains. The papers in Part VI focus on wild mice, covering their classification and biochemical polymorphisms. Finally, Part VIII discusses the viruses, T locus, and histocompatibility antigens of wild mice.

Origins of Inbred Mice

This major work, complete with 150 illustrations, many of them in color, bridges the gap between clinical pulmonary pathology and basic molecular science. Through a highly visual approach that features an abundance of tables and diagrams, the book offers a practical disease-based overview. The first two sections of the volume provide the reader with general concepts, terminology and procedures in molecular pathology. The remainder of the volume is subdivided into neoplastic and non-neoplastic lung diseases with detailed chapters covering the current molecular pathology of specific diseases. The book will be essential reading for pathologists, pulmonologists, thoracic surgeons and other health care providers interested in lung disease.

Molecular Pathology of Lung Diseases