Original Article Angiogenic And Innate Immune Responses

Cardiovascular immunology is a newly emerging research area, investigating the crosstalk between the cardiovascular and the immune system. This crosstalk is evident through (1) crucial immunological capacities and functions of cardiovascular cell types, including cardiomyocytes, fibroblasts, endothelial cells, pericytes and cardiac resident macrophages, (2) the impact of aberrant immune function on the development of cardiovascular disease such as atherosclerosis, direct and indirect immune-mediated heart disease and vasculitis, and (3) the crucial role of the immune system in cardiac repair and regeneration. The Immunology of Cardiovascular Homeostasis and Pathology covers all these aspects of cardiovascular immunology, starting with homeostatic immunological functions of traditional cardiovascular cell types, and moving then to the role of the immune system in cardiovascular pathology and to recent research into targeting the immune system to boost cardiac healing and regeneration.
This selection of articles from the Encyclopedia of the Eye provides a comprehensive overview of immunological features, diseases and inflammation of the eye and its support structures and organs. Rather than taking an immunological focus that is strictly suitable for clinicians, the volume offers a considerable basic science background and addresses a broad range of topics - the immune system of the eye, its various disorders, mechanisms of inflammation of the eye and visual system, treatment, wound healing mechanisms, stem cells, and more. The first single volume to integrate comparative studies into a comprehensive resource on the neuroscience of ocular immunology Chapters are carefully selected from the Encyclopedia of the Eye by the world's leading vision researchers The best researchers in the field provide their conclusions in the context of the latest experimental results
This comprehensive text provides a detailed overview of the molecular mechanisms underpinning the development of cancer and its treatment. Written by an international panel of researchers, specialists and practitioners in the field, the text discusses all aspects of cancer biology from the causes, development and diagnosis through to the treatment of cancer. Written by an international panel of researchers, specialists and practitioners in the field Covers both traditional areas of study and areas of controversy and emerging importance, highlighting future directions for research Features up-to-date coverage of recent studies and discoveries, as well as a solid grounding in the key concepts in the field Each chapter includes key points, chapter summaries, text boxes, and topical references for added comprehension and review Supported by a dedicated website at www.blackwellpublishing.com/pelengaris An excellent text for upper-level courses in the biology of cancer, for medical students and qualified practitioners preparing for higher exams, and for researchers and teachers in the field
The Mononuclear Phagocyte System (MPS) of vertebrates is composed of monocytes, macrophages and dendritic cells. Together, they form part of the first line of immune defense against a variety of pathogens (bacteria, fungi, parasites and viruses), and thus play an important role in maintaining organism homeostasis. The mode of transmission, type of replication and mechanism of disease-causing differ significantly for each pathogen, eliciting a unique immune response in the host. Within this context, the MPS acts as both the sentinel and tailor of the immune system. As sentinels, MPS cells are found in blood and within tissues throughout the body to patrol against pathogenic insult. The strategy to detect 'microbial non-self' relies on MPS to recognize conserved microbial products known as 'pathogen-associated molecular pattern' (PAMPs). PAMPs recognition represents a checkpoint in the response to pathogens and relies on conserved 'pattern recognition receptors' (PRRs). Upon PRR engagement, MPS mount a cell-autonomous attack that includes the internalization and compartmentalization of intracellular pathogens into toxic compartments that promote destruction. In parallel, MPS cells launch an inflammatory response composed of a cellular arm and soluble factors to control extracellular pathogens. In cases when innate immunity fails to eliminate the invading microbe, MPS serves as a tailor to generate adaptive immunity for pathogen eradication and generation of "memory" cells, thus ensuring enhanced protection against re-infection. Indeed, MPS cell functions comprise the capture, process, migration and delivery of antigenic information to lymphoid organs, where type-1 immunity is tailored against intracellular microbes and type-2 immunity against extracellular pathogens. However, this potent adaptive immunity is also a double-edge sword that can cause aberrant inflammatory disorders, like autoimmunity or chronic inflammation. For this reason, MPS also tailors tolerance immunity against unwanted inflammation. Successful clearance of the microbe results in its destruction and proper collection of debris, resolution of inflammation and tissue healing for which MPS is essential. Reciprocally, as part of the evolutionary process taking place in all organisms, microbes evolved strategies to circumvent the actions bestowed by MPS cells. Multiple pathogens modulate the differentiation, maturation and activation programs of the MPS, as an efficient strategy to avoid a dedicated immune response. Among the most common evasion strategies are the subversion of phagocytosis, inhibition of PRR-mediated immunity, resistance to intracellular killing by reactive oxygen and nitrogen species, restriction of phagosome maturation, modulation of cellular metabolism and nutrient acquisition, regulation of cell death and autophagy, and modulation of pro-inflammatory responses and hijacking of tolerance mechanisms, among others. The tenet of this eBook is that a better understanding of MPS in infection will yield insights for development of therapeutics to enhance antimicrobial processes or dampen detrimental inflammation for the host's benefit. We believe that contributions to this topic will serve as a platform for discussion and debate about relevant issues and themes in this field. Our aim is to bring expert junior and senior scientists to address recent progress, highlight critical knowledge gaps, foment scientific exchange, and establish conceptual frameworks for future MPS investigation in the context of infectious disease.
Tumor Vascularization discusses the different types of growth of tumor blood vessels and their implications on research and healthcare. The book is divided into three parts: the first one, General Mechanisms, discusses different vessel growth mechanisms, such as sprouting angiogenesis, non-angiogenesis dependent growth, intussusceptive microvascular growth, vascular co-option and vasculogenic mimicry. The second and third parts, entitled Clinical Implications and Therapeutic Implications are dedicated to translating recent findings in this field to patient treatment and healthcare. This book is a valuable source for cancer researchers, oncologists, graduate students and members of the biomedical field who are interested in tumor progression and blood vessels. Explains new, non-orthodox concepts recently developed and related to the modality of growth of tumor blood vessels Provides information on the types of angiogenesis, non-angiogenesis dependent growth and vascular co-option, discussing both their similarities and differences Encompasses a discussion on clinical implications of tumor vascularization to translate research findings into treatment
The inflammasome was first described in 2002 as a molecular complex activating proinflammatory caspases and therefore regulating the maturation and biological activities of cytokines such as IL-1? and IL-18. This finding was substantiated by the identification of several mutations in the cias1 gene, encoding the human NLRP3 protein, responsible for several autoinflammatory disorders such as the Muckle Wells syndrome. Since, the interest for this complex has constantly increased and several inflammasome complexes with different specificities have been described. These inflammasomes sense a wide variety of pathogens and danger signals and are key players in the inflammatory response. With the contributions of leading international experts in the field, this book provides an extensive overview of the current knowledge of inflammasome biology and their role in health and disease.
We acknowledge the initiation and support of this Research Topic by the International Union of Immunological Societies (IUIS). We hereby state publicly that the IUIS has had no editorial input in articles included in this Research Topic, thus ensuring that all aspects of this Research Topic are evaluated objectively, unbiased by any specific policy or opinion of the IUIS. Part of the APCs for articles in this collection were financed by the Fondazione Beppe e Nuccy Angiolini ONLUS. Publisher’s note: In this 2nd edition, acknowledgment for the Fondazione Beppe e Nuccy Angiolini ONLUS has been added.

For long, high dose ionizing radiation was considered as a net immune suppressing agent, as shown, among others, by the exquisite radiosensitivity of the lymphoid system to radiation-induced cell killing. However, recent advances in radiobiology and immunology have made this picture more complex. For example, the recognition that radiation-induced bystander effects, share common mediators with various immunological signalling processes, suggests that they are at least partly immune mediated. Another milestone was the finding, in the field of onco-immunology, that local tumor irradiation can modulate the immunogenicity of tumor cells and the anti-tumor immune responsiveness both locally, in the tumor microenvironment, and at systemic level. These observations paved the way for studies exploring optimal combinations of radiotherapy and immunotherapy in order to achieve a synergistic effect to eradicate tumors. However, not all interactions between radiation and the immune system are beneficial, as it was recognized that many of radiation-induced late side effects are also of immune and inflammatory nature. Currently perhaps the most studied field of research in radiation biology is focused around the biological effects of low doses, where many of the observed pathophysiological endpoints are due to mechanisms other than direct radiation-induced cell killing and are immune-related. Finally, it must not be forgotten that the interactions between the ionizing radiations and the immune system are bi-directional, and activation of the immune system also influences the outcome of radiation exposure. This Research Topic brings together 23 articles and aims to give an overview of the complex and very often contradictory nature of the interactions between ionizing radiation and the immune system. Due to its increasing penetrance in the population both through medical diagnostic or environmental sources or during cosmic travel low dose ionizing radiation exposure is becoming a major epidemiological concern world-wide. Several of the articles within the Research Topic specifically address potential long-term health consequences and the underlying mechanisms of low dose radiation exposure. A major intention of the Editors was also to draw the attention of the non-radiobiological scientific community on the fact that ionizing radiation is by far more than purely an immune suppressing agent.

Macrophages are the sentinels of the immune system whose role has evolved beyond providing aseptic conditions to homeostasis, immune regulation, development, and behaviour. These cells have varied ontogenetic origins which reflects in their phenotypic and functional heterogeneity. Macrophage functions are fine-tuned by exogenous and endogenous signals and once tweaked, the information is included in their genetic makeup, albeit not indefinitely. Subversion of the macrophage functions is the hallmark of many pathogenic organisms and modulation of macrophage activity is pivotal to many therapeutic strategies. Fascinating and rapid developments in this field have necessitated the maintenance of currency of knowledge. This book provides a current account of information on varied topics in macrophage biology. Literature surveys have been presented in a captivating and lucid language. The contributing authors have also provided brief accounts of their own research. Every chapter provides a future perspective of what more could be achieved in the context of the current knowledge. The book will be of interest to students and researchers in microbiology, immunobiology, translational research, pathology, and related fields.

Kidney cancer imposes a significant cancer burden and its incidence continues to rise globally. Mortality in advanced kidney cancer remains high despite oncological, surgical and multimodal optimisation. Genetic associations, heterogeneity and limitations in early diagnosis through lack of optimal biomarkers add to the challenges. Over the last two decades there has been an exponential increase in diagnostic and therapeutic advances in the management of kidney cancer. The coupling of scientific advances in engineering and technology with oncological therapeutics has recently ushered a renewed optimism. The role of minimally invasive approaches through focal therapy and surgical extirpation using the robotic platform has been unprecedented and paramount. Virtual augmentation and mixed reality platforms have proved useful supplementary tools in surgical planning. The role of surgical simulation and training in development of surgeons with the optimal skill set is essential to provide optimal care. This book is the first in a series that explores the evolving trends in kidney cancer. The focus of the book is broad and includes topics ranging from immunotherapy to surgical simulation. Some chapters explore leading edge concepts while others capture the evolving trends and future concepts. The Editors aim to stimulate the readers to explore the key concepts and to encourage research and innovation along the main themes presented.

Angiogenesis is the physiological process where new blood vessels grow from existing ones, in order to replenish tissues suffering from inadequate blood supply. Perhaps the most studied angiogenic process occurs in solid tumors whose growing mass and expanding cells create a constant demand for additional supply of oxygen and nutrients for survival. However, other physiological and clinical conditions, such as wound healing, ischemic events, autoimmune and age-related diseases also involve angiogenesis. Angiogenesis is a well-structured process that begins when oxygen and nutrients are depleted, leading to the release of chemokines and growth factors that attract immune cells, particularly macrophages and endothelial cells to the site. Macrophages that are recruited to the site, as well as tissue cells and endothelial cells, secrete pro-angiogenic mediators that affect endothelial cells and promote angiogenesis. These mediators include growth factors such as vascular endothelial cell growth factor (VEGF), matrix metalloproteinases (MMPs), as well as low levels of mediators that are usually seen as pro-inflammatory but are pro-angiogenic when secreted in low levels (e.g. nitric oxide (NO) and TNFa). Thus, macrophages play a major role in angiogenesis. Macrophages exhibit high plasticity and are capable of shifting between different activation modes and functions according to their changing microenvironment. Small differences in the composition of activating factors (e.g. TLR ligands such as LPS, anti-inflammatory cytokines, ECM molecules) in the microenvironment may differently activate macrophages to yield classically activated macrophages (or M1 macrophages) that can kill pathogen and tumor cells, alternatively activated macrophages (or M2 macrophages) that secrete antiinflammatory cytokines, resolution macrophages (rM?) that are involved in the resolution of inflammation, or regulatory macrophages (e.g. Myeloid-Derived Suppressor Cells - MDSCs) that control the function of other immune cells. In fact, macrophages may be

activated in a spectrum of subsets that may differently contribute to angiogenesis, and in particular non-classically activated macrophages such as tumor-associated macrophages (TAMs) and Tie2-expressing monocytes (TEMs) can secrete high amounts of pro-angiogenic factors (e.g. VEGF, MMPs) or low levels of pro-inflammatory mediators (e.g. NO or TNFa) resulting in pro-angiogenic effects. Although the importance of macrophages as major contributors and regulators of the angiogenic process is well documented, less is known about the interactions between macrophages and other cell types (e.g. tumor cells, normal epithelial cells, endothelial cells) that regulate angiogenesis. We still have only limited understanding which proteins or complexes mediate these interactions and whether they require cell-cell contact (e.g. through integrins) or soluble factors (e.g. the EGF-CSF-1 loop), which signaling pathways are triggered in each of the two corresponding cell types, and how this leads to secretion of pro- or antiangiogenic factors in the microenvironment. The regulation of such interactions and through them of angiogenesis, whether through post-translational modifications of proteins or via the involvement of microRNA, is still unclear. The goal of this Research Topic is to highlight these interactions and their regulation in the context of both physiological and pathological conditions.

Once viewed solely as fat storage cells, adipocytes and their adipokines have now been proven to be central for human health. Understanding that overweight and obesity may increase the risk for various diseases requires detailed characterization of adipokine function. Weight gain, weight regain, and fasting affect adipocyte health and accordingly their secretome. Different adipose tissue deposits exist and they vary in cellular composition and function. The evidence is strong of a role of adipokines in cancer, reproductive function, neurological diseases, cardiovascular diseases ,and rheumatoid arthritis. Adipokines are considered useful biomarkers for adipose tissue and metabolic health, and may be used as diagnostic tools in rheumatoid arthritis, cancer, or sepsis. This book contains 10 original articles and 9 review articles focusing on these bioactive peptides. Several articles deal with chemerin, an adipokine discovered more than 20 years ago. Data so far have resulted in promising insights related to its biological function. We are only beginning to understand the multiple roles of chemerin, the mechanisms regulating its activity, and the signaling pathways used by this chemokine. Adipokine receptor agonists and antagonists may result in the formulation of novel drugs and ultimately may lead to new therapeutic targets to be used in clinical practice.

Natural Killer (NK) cells are large granular lymphocytes of the innate immune system. They are widespread throughout the body, being present in both lymphoid organs and non-lymphoid peripheral tissues. NK cells are involved in direct innate immune reactions against viruses, bacteria, parasites and other triggers of pathology, such as malignant transformation, all of which cause stress in affected cells. Importantly, NK cells also link the innate and adaptive immune responses, contributing to the initiation of adaptive immune responses and executing adaptive responses using the CD16 FcgRIIIA immunoglobulin Fc receptor. Such responses are mediated through two major effector functions, the direct cytolysis of target cells and the production of cytokines and chemokines. The authors focus here on the nature of recognition events by NK cells and address how these events are integrated to trigger these distinct and graded effector functions.

Biochemical Toxicology - Heavy Metals and Nanomaterials provides an overview of biochemical contamination, nanomaterials and toxic metals, and measurement techniques. It explains and clarifies important studies and compares and develops new and groundbreaking measurement techniques in the fields of organic and inorganic pollution and nanoscience. It is highly recommended for professionals and readers interested in the environment and human health.

Architecture and Control addresses the urgent question residing at the intersection of architectural and cultural theory: how can the interplay between designed structures and practices of control foster an emergence of the unforeseen and the uncontrolled in post-2000 architectures and infrastructures?

Transcription depends on an ordered sequence of events, starting with (i) setting of the enhancer and chromatin environment, (ii) assembly of DNA binding and general transcription factors, (iii) initiation, elongation, processing of mRNA and termination, followed by (iv) creation of epigenetic marks and memory formation. Highlighting the importance of these activities, more than 10% total genes are dedicated to regulating transcriptional mechanisms. This area of research is highly active and new insights are continuously being added to our knowledge. Cells of the immune system have unique features of gene regulation to support diverse tasks required for innate and adaptive immunity. Innate immunity involves the recognition of external infectious and noxious agents as well as internal cancer cell components, and the elimination of these agents by non-specific mechanisms. Adaptive immunity involves gene rearrangement to achieve highly specific T and B cell responses, imparting the capability of self and non-self discrimination. This requires transcription and epigenetic regulation. Adaptive immunity also employs epigenetic memory, enabling recapitulation of prior transcription. Recent advances in nuclear architecture, chromatin structure, and transcriptional regulation have provided new insights into immune responses. The increased understanding of these molecular mechanisms is now affording opportunities to improve therapeutic strategies for various diseases.

This book addresses the background and significance of the factors potentially influencing the clinical and biological outcomes of metal-on-metal hip implants. Metal-on-metal bearings were introduced and evaluated as an alternative to other bearing couples, particularly metal-on-polyethylene, due to their enhanced wear resistance as determined in laboratory testing. Initially, reports of short-term clinical outcomes were favorable and an increasing number of metal-on-metal prostheses were implanted. Subsequently, isolated case findings describing adverse tissue responses around the articulation became the harbinger of an increasing number of reports describing pseudotumors and other significant lymphocytic-based responses associated with metal-on-metal prostheses. Questions have been raised as to whether this is an implant, design, or patient-specific response. The reasons why some patients have a negative biological response and pathology while others do not remain to be determined, but tens of thousands of patients in

the US, the UK, and around the world are considered to be at risk. Leading researchers and clinicians describe the issues related to the nature of the biological and pathological responses and the protocols that should be followed to determine if an adverse response is occurring. This book is essential reading for researchers, engineers, and orthopaedic surgeons who are involved in the design, evaluation, and implantation of metal-on-metal prostheses.

This book is a continuation of the efforts of InTech to expand the scientific know-how in the field of immunopathology and bring valuable updated information to medical professionals and researchers. It consists of chapters related to various approaches to investigate the unique role of the immune system in response to different clinical disorders. The international team of authors is the bonus of the book, reflecting the rapid development of immunology and new achievements in medical science. We firmly hope that the book will be an excellent manual and guideline for people dealing with biology, microbiology, immunology, virology, pharmacology, general and dental medicine, and health care, from students and postdocs to high-level specialists and university professors.

Gene therapy, bioengineered skin, and other methods in advanced biology are revolutionizing the treatment of wounds. Written by experts in research and clinical practice, Cutaneous Wound Healing examines the current knowledge and emerging treatment methods. This volume explains the normal molecular and cellular functions that occur when a wound heals, as well as dysfunctional events, such as a chronic wound or an ulcer. Such dysfunctions signal an imbalance in the body, explained here along with possible treatments. The book's mini-atlas is an indispensable reference tool. Dermatologists, plastic surgeons, and general practitioners can benefit from this text.

Tumor-Induced Immune Suppression - Prospects and Progress in Mechanisms and Therapeutic Reversal presents a comprehensive overview of large number of different mechanisms of immune dysfunction in cancer and therapeutic approaches to their correction. This includes the number of novel mechanisms that has never before been discussed in previous monographs. The last decades were characterized by substantial progress in the understanding of the role of the immune system in tumor progression. Researchers have learned how to manipulate the immune system to generate tumor specific immune response, which raises high expectations for immunotherapy to provide breakthroughs in cancer treatment. It is increasingly clear that tumor-induced abnormalities in the immune system not only hampers natural tumor immune surveillance, but also limits the effect of cancer immunotherapy. Therefore, it is critically important to understand the mechanisms of tumor-induced immune suppression to make any progress in the field and this monograph provides these important insights.

Volume 12 of the world-renowned Trophoblast Research series, devoted to placental science.

This book is focused on the analysis of the role played by immune cell components in the angiogenic process associated with inflammation and tumor growth. Both innate and adaptive immune cells are involved in the mechanisms of endothelial cell proliferation, migration and activation, through the production and release of a large spectrum of pro-angiogenic mediators. These may create the specific microenvironment that favors an increased rate of tissue vascularization. The link between chronic inflammation and tumorigenesis was first proposed by Rudolf Virchow in 1863 after the observation that infiltrating leukocytes are a hallmark of tumors and first established a causative connection between the lymph reticular infiltrate at sites of chronic inflammation and the development of cancer. Tumors were described as wounds that never heal and surgeons have long described the tendency of tumors to recur in healing resection margin and it has been reported that wound healing environment provides an opportunistic matrix for tumor growth. As angiogenesis is the result of a net balance between the activities exerted by positive and negative regulators, this book will also provide information on some anti-angiogenic properties of immune cells that may be utilized for a potential pharmacological use as anti-angiogenic agents in inflammation as well as in cancer. The work is written for researchers in the field and also for graduate students which approach this matter.

Angiogenesis describes the formation of new blood vessels, which arise as outgrowths from existing vessels. In many physiological processes such as ovulation and wound healing angiogenesis is involved for a relatively short time. Otherwise under normal physiological conditions in the adult organism angiogenesis is an extremely slow process. By contrast in certain disease states such as diabetic retinopathy, arthritis, chronic inflammation, hemangiomas, etc., angiogenesis persists and contributes to the pathology of these disease states. Some 50 such "angiogenic diseases" have been described where angiogeneSiS is involved. Also in tumor growth and metastasis angiogenesis is an essential process and precedes neoplastic transformation. Hence, angiogenesis could become an important diagnostic tool and a target for developing therapeutic agents. This book contains the proceedings of the NATO Advanced Study Institute on "Angiogenesis in Health and Disease" held in Porto Hydra, Greece, from June 16-27, 1991. This meeting was a comprehensive review of endothelial cell biology and endothelial cell phenotypic and functional heterogeneity in relation to angiogenesis under physiological and pathological conditions. Numerous in vitro and in vivo models were presented, which are used to study angiogenesis at the molecular and cellular levels and to evaluate chemical compounds or naturally occuring substances for their effect on angiogenesis. The presentations and discussions at this meeting provided an opportunity for the basic science and the clinical disciplines to meet, exchange information and provide future research directions for many investigators engaged in the study of angiogenesis.

Covers the topic of collateral circulation and its structure and function; its molecular mechanisms during the course of critical arterial stenosis; and how it can be stimulated by physical and growth factors. Animal models are covered in this volume as they reproduce the clinical situation in the laboratory. The book also contains mechanistic explanations of vascular growth that are reflected in numerous charts.

Poststructuralism, particularly through the writings of Michel Foucault and Judith Butler, has achieved remarkable success in challenging our belief in natural sex categories and

instincts. Here, Carrie Hull endorses the progressive ideals of poststructuralism while demonstrating the superiority of a realist account of sex and sexuality. Embracing biological and cultural variability, Hull nonetheless shows that the sexed body is naturally structured and deeply meaningful. Poststructuralist philosophers have argued that biological sex is a continuum rather than a binary, and that sex identity and drive are entirely performances of cultural norms rather than expressions of innate qualities. Hull draws parallels with Nelson Goodman, W.V.O. Quine, and B.F. Skinner to show that these poststructuralist theories are rooted in a nominalist, relativist, and behaviourist philosophy, and develops an alternative framework using arguments from contemporary and critical realism. Employing colourful illustrations from biology, anthropology and psychology, Hull demonstrates the rich potential of realist philosophy, and concludes that it is philosophically and scientifically correct, on one hand, and politically advisable, on the other, to maintain a distinction - albeit attenuated - between sex and gender, and sexuality and behaviour.

This book provides readers with an up-to-date and comprehensive view on the resolution of inflammation and on new developments in this area, including pro-resolution mediators, apoptosis, macrophage clearance of apoptotic cells, possible novel drug developments.

Rev. ed. of: Acute and chronic wounds / [edited by] Ruth A. Bryant, Denise P. Nix. 3rd ed. c2007.

In the past, neutrophils were often reduced to their ability to release preformed mediators and kill pathogens. The present volume of Chemical Immunology and Allergy, however, offers a very broad and timely view by highlighting the versatile functions of neutrophils in inflammatory, immune and antitumoral responses. Leading investigators uncover novel aspects of neutrophils, such as their capacity to control gene expression at the transcriptional level, or respond to proinflammatory cytokines, cytokine receptor chains (gc) and endogenous anti-inflammatory lipid mediators. Further points under discussion are neutrophils presenting antigens, activating T cells, participating in chemokine networking, and producing IL-12 and other cytokines during infectious diseases. Among the most original findings presented in this publication figure the observations that neutrophils cause increased vascular permeability during acute inflammation, regulate directly the angiogenic process, and influence tumor development. A final article offers a detailed description of the molecular processes affecting neutrophil cell death and survival. Unique in its field, this valuable volume is recommended reading not only for immunologists and pathologists, but also for cell biologists, hematologists and immunobiologists.

Pancreatic ribonuclease, the focus of highly productive scientific research for more than half a century and the only enzyme to be the basis of four Nobel prizes, has recently undergone a resurgence in popularity for the recognition of an extended ribonuclease superfamily with functions ranging from tumour growth and inhibition to self-recognition and neurotoxicity. This volume highlights the functional diversity of ribonucleases and reveals the emerging research opportunities provided by these enzymes. * Never before has discussion of the entire family of ribonucleases and related enzymes been covered in a single volume * Core chapters focus on the latest structures and functions of pancreatic-type ribonucleases * Structures and functions of intracellular ribonucleases and nondigestive members of the family are also covered * How ribonucleases continue to serve as excellent systems with which to uncover the secrets of protein chemistry is demonstrated

Tumor angiogenesis is one of the most prominent mechanisms driving tumor development and progression. This book is written by internationally renowned experts. Part 1 describes the basic mechanisms. Tumor-angiogenic signaling pathways are presented as new potential targets for anti-angiogenic therapy. Part 2 reviews the efforts made to validate new targets and to show efficacy in animals. Part 3 is devoted to the clinical development of the novel anti-angiogenic drugs and their use in clinical practice.

Angiogenesis, Lymphangiogenesis and Clinical ImplicationsKarger Medical and Scientific Publishers

Angiogenesis, the formation of new blood vessels, is fundamental for physiological processes such as embryonic and postnatal development, wound repair, and reproductive functions. Angiogenesis plays a major role in tumor growth and in several autoimmune and allergic disorders. Lymphangiogenesis, the formation of new lymphatic vessels, is also important for tumor growth, the formation of metastasis, and chronic inflammatory diseases. Judah Folkman, a pioneer in the study of angiogenesis, first proposed that macrophages and mast cells could be a relevant source of angiogenic factors. Since then, much effort has gone into the elucidation of the role of immune cells in the modulation of angiogenesis and lymphangiogenesis. There is now compelling evidence that several components of the innate and adaptive immune system are implicated in inflammatory and neoplastic angiogenesis and lymphangiogenesis. Articles in this volume deal with the emerging, intriguing possibility that immune cells are both a source and a target of angiogenic and lymphangiogenic factors. Therefore, cells of the immune system might play a role in inflammatory and neoplastic angiogenesis/lymphangiogenesis through the expression of several angiogenic factors and their receptors and co-receptors. The important new findings in this volume will be of special interest to vascular biologists, basic and clinical immunologists, oncologists and to specialists in allergic and immune disorders.

We acknowledge the initiation and support of this Research Topic by the International Union of Immunological Societies (IUIS). We hereby state publicly that the IUIS has had no editorial input in articles included in this Research Topic, thus ensuring that all aspects of this Research Topic are evaluated objectively, unbiased by any specific policy or opinion of the IUIS.

Angiogenesis, the development of new blood vessels from the existing vasculature, is essential for physiological growth and over 18,000 research articles have been published describing the role of angiogenesis in over 70 different diseases, including cancer, diabetic retinopathy, rheumatoid arthritis and psoriasis. One of the most important technical challenges in such studies has been finding suitable methods for assessing the effects of regulators of eh angiogenic response. While increasing numbers of angiogenesis assays are being described both in vitro and in vivo, it is often still necessary to use a combination of assays to identify the cellular and molecular events in angiogenesis and the full range of effects of a given test protein. Although the endothelial cell - its migration, proliferation, differentiation and structural rearrangement - is central to the angiogenic process, it is not the only cell type involved. the supporting cells, the extracellular matrix and the circulating blood with its cellular and humoral components also contribute. In this book, experts in the use of a diverse range of assays outline key components of these and give a critical appraisal of their strengths and weaknesses. Examples include assays for the proliferation, migration and differentiation of endothelial cells in vitro, vessel outgrowth

from organ cultures, assessment of endothelial and mural cell interactions, and such in vivo assays as the chick chorioallantoic membrane, zebrafish, corneal, chamber and tumour angiogenesis models. These are followed by a critical analysis of the biological end-points currently being used in clinical trials to assess the clinical efficacy of anti-angiogenic drugs, which leads into a discussion of the direction future studies should take. This valuable book is of interest to research scientists currently working on angiogenesis in both the academic community and in the biotechnology and pharmaceutical industries. Relevant disciplines include cell and molecular biology, oncology, cardiovascular research, biotechnology, pharmacology, pathology and physiology.