

# New horizons in platelet research: Understanding and harnessing platelet functional diversity

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**Abstract.** Recent years have been ripe with discoveries of non-haemostatic platelet functions. This led to the appreciation of the significant, previously unknown, role played by the platelets in various pathologies and regenerative processes. As a result, exciting opportunities for clinical applications in fields as diverse as regenerative medicine and cancer treatment are emerging. However, their realization depends on the understanding of the regulatory mechanisms governing these diverse platelet functions, so that particular platelet responses could be artificially tailored to specific clinical situations. Current understanding of the signalling pathways controlling haemostatic responses is rooted in the development of quantitative assays for measuring them and sensitive markers for their quantification. However, the existing assays and markers are not sufficiently sensitive for distinguishing between individual signalling pathways and unravelling inter-pathway connections. Moreover, entirely new approaches are needed for studying non-haemostatic platelet functions, since there are currently no assays or markers for quantifying them. We review the on-going efforts in these directions, including our own recent work on using lectins as sensitive probes for profiling platelet activation.

## 1. Platelets and their therapeutic potential

Last decade in platelet research has been ripe with exciting surprises. Originally thought of as clotting factories (Fig. 1), platelets turned out to be involved in a wide variety of physiological and pathophysiological processes [75]. They appear to function as a Swiss army knife, unsheathed as a first-response to injury, in processes ranging from coagulation, where they limit traumatic blood loss, to inflammation and the subsequent steps of the wound healing cascade [5, 88, 97], angiogenesis [88, 96], vascular remodelling and maintenance of vascular integrity [35], *de novo* blood vessel synthesis, initial response to pathogens [148], and other aspects of both innate and adaptive immune response (Fig. 2) [88, 121, 138]. Misfiring of these mechanisms is implicated in pathological conditions as diverse as atherosclerosis [13, 67, 78, 110] and the development of cancer metastases [33, 34, 127]. This diversity raises important questions but also presents therapeutic opportunities that are as unique as they are varied. The realization of these opportunities is predicated on the understanding of the regulatory processes that govern platelets' various functional roles.

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# New Horizons In Platelet Activating Factor Research

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## **New Horizons In Platelet Activating Factor Research:**

New Horizons in Platelet Activating Factor Research C. M. Winslow, Mark L. Lee, 1987 Platelet Activating Factor PAF is a naturally occurring substance with potent biological effects which have a broad significant role in the activation of various inflammatory cells. It therefore contributes to a number of serious clinical conditions including anaphylaxis, allergic and inflammatory diseases eg asthma, rhinitis, thrombosis. This book brings together leading investigators in the field to present their latest research directed towards the biosynthesis of PAF, its cellular origins, PAF induced cellular and tissue responses, pathophysiological responses and most important to finding effective antagonistic drugs to control this inflammatory mediator.

**Platelet-Activating Factor and Related Lipid Mediators** F. Snyder, 2013-11-11 Platelet activating factor PAF is the commonly used name for a group of potent biologically active ether linked phospholipids, the alkylacetyl glycerophosphocholines. Following the identification of the chemical structure of PAF in 1979, much progress has been made in our understanding of these phospholipid mediators. This is particularly true from the points of view of their molecular structural requirements for expression of biological activity, their biosynthesis and catabolism, their diverse range of biological activities, evidence for their specific receptors at the cell surface, the development of specific antagonists for use in receptor studies and for testing as potential anti-PAF drugs and implications about their involvement in health and disease. Chapters in this book cover the current status of these general areas of PAF research. Although an enormous amount of information has been published about this interesting new type of phospholipid mediators, questions about their mechanism of action, regulatory controls and the precise role and relative importance of PAF in specific diseases and physiological functions remain to be answered. Since the 1979 discovery, the PAF field has brought together scientists from a variety of different biomedical disciplines. The diversity of scientists now in PAF research is very apparent from the number of PAF publications appearing in a wide array of scientific journals ranging from molecular biology to clinical medicine. Publications related to PAF continue to increase at an amazingly rapid rate with the pace reminiscent of the period following the discovery of prostaglandins.

**Molecular Mechanisms of Neuronal Responsiveness** Yigal H. Ehrlich, Robert H. Lenox, Elizabeth Kornecki, William O. Berry, 2013-03-13 The interaction of neurotransmitters, neuromodulators and neuroactive drugs with receptors localized at the cell surface initiates a chain of molecular events leading to integrated neuronal responses to the triggering stimuli. Major advancements in the characterization and isolation of receptor molecules have answered many questions regarding the nature of the elements that determine the specificity in these interactions. At the same time, recent studies have provided evidence that delicate regulation by intracellular enzymatic systems determines the efficiency of the stimulus response coupling process. Mediation of the interaction between receptors operates in feedback control mechanisms and transduces signals from the receptors to various effector sites in a highly coordinated fashion. These studies are at the focus of the present volume, which is an outcome of a symposium held at the University of Vermont College.

of Medicine on March 21-23, 1986 in conjunction with the seventeenth annual meeting of the American Society for Neurochemistry. The symposium has demonstrated clearly that the concerted efforts of investigators in neurophysiology, biochemistry, pharmacology, cell biology, molecular genetics, neurology, and psychiatry are required to achieve better understanding of the processes underlying neuronal responsiveness. This volume includes contributions provided by prominent investigators in all these research areas. We hope that the readers will find here a useful source of information and ideas for stimulating further studies which may serve to narrow the gap between basic neuroscience research and its clinical implications.

*Lipid Mediators* Fiona M. Cunningham, 2016-10-27. The Handbook of Immunopharmacology: Lipid Mediators covers a comprehensive overview of lipid mediators from synthesis through to inhibition. The book discusses the metabolism of arachidonic acid, the measurement of fatty acids and their metabolites, and the biological properties of cyclooxygenase products. The text also describes other essential fatty acids, their metabolites, and cell-cell interactions, the inhibitors of fatty acid-derived mediators, as well as the biosynthesis and catabolism of platelet-activating factor. The cellular sources of platelet-activating factor and related lipids, the biological properties of platelet-activating factor, and the effects of platelet-activating factor receptor antagonists are also considered. Immunopharmacologists, immunologists, and pharmacologists will find the book invaluable.

*Arachidonate Metabolism in Immunologic Systems* L. Levine, 1988. **Aliphatic Compounds** Malcolm Sainsbury, 2016-06-24. Rodd's Chemistry of Carbon Compounds, Volume I: Aliphatic Compounds focuses on the chemistry of polyhydric alcohols and saccharides. The chemistry of polyhydric alcohols is a vast and crucially important area not only because of the prominent roles that polyols have in their own right but because of the way they and their modified forms are incorporated into natural products. The topics covered include the analogues, derivatives, and oxidation products of trihydric and tetrahydric alcohols, phospholipids, polyhydric alcohols, and their oxidation products; synthesis, chemistry, structure, and physical properties; and use in the synthesis as chiral templates and asymmetric synthesis of natural products of monosaccharides and disaccharides and oligosaccharides. This text also discusses the applications of carbohydrates as chiral auxiliaries, templates, and starting materials in syntheses. This volume is a useful reference for students and organic chemists.

*Principles of Cell Adhesion* (1995) Peter D. Richardson, Manfred Steiner, 2017-11-22. Intended for cell biologists, biophysicists, biochemists, molecular biologists, physiologists, researchers in hemostasis and thrombosis, and pathologists, this book provides an insight into cell adhesion from three interdisciplinary perspectives: fundamental facts of adhesion, molecular biochemistry of adhesion, and physiological aspects. It summarizes the basic aspects of surfaces in general and describes the theoretical and experimental tools necessary to investigate cell adhesion, including the basic biochemistry and molecular biology of adhesion. The book offers concise treatment of individual topics, features current material, and provides key references as a guide to further study.

*Inflammation* Robert R. Ruffolo, Jr., Manfred A. Hollinger, 1995-06-21. *Inflammation: Mediators and Pathways* reviews key developments in the field of inflammation. It focuses on novel pathways of

inflammation that have only recently surfaced All the topics covered are currently the subject of intense investigation and all contributors are established investigators in the field

**Handbook of Mucosal Immunology**, 2012-12-02 Researchers have recently made tremendous progress in the area of mucosal immunology greatly increasing our understanding of the common mucosal immune system mucosal infections and oral immunization However this research has not previously been made available in a single work In its large 81 2x 11 format Handbook of Mucosal Immunology covers the entire spectrum of mucosal immunity and is organized in two main sections to present the basic biology of the common mucosal immune system and the immune responses of the mucosae The first section provides an introduction and historical perspective of the mucosal immune system and includes comprehensive discussion of the development and physiology of mucosal defense It discusses such topics as the structure and function of the mucosal epithelium characteristics of mucosal associated lymphoid tissue MALT Peyer's patches and concepts of mucosal vaccines The second section focuses on the secretory immune system with special reference to mucosal diseases in the digestive GALT respiratory BALT and genitourinary tracts This information is especially important in light of the current interest in the mechanisms transmission and prevention of infectious diseases such as AIDS hepatitis and tuberculosis Virtually all chapters have been authored by the original investigators responsible for key observations on which current concepts are based This handbook will be an invaluable resource for a diverse group of both researchers and practicing clinicians Molecular biologists immunologists veterinarians public health workers physicians in specialties from pediatrics to pulmonology and graduate students of mucosal immunology will all find this handbook the most complete work on the subject

*National Library of Medicine Current Catalog* National Library of Medicine (U.S.), 1987

**Handbook of PAF and PAF Antagonists** | Pierre Braquet, 2019-06-13 Published in 1991 Since its characterization in the 1970s from antigen stimulated rabbit basophils platelet activating factor PAF has been demonstrated to be produced by and act upon a variety of cell types PAF antagonists which have been obtained from both natural sources and chemical synthesis now represent a new class of therapeutic agents and may provide new prospects for treating several major pathologies particularly shock ischemia and asthma This book provides a unique overview of the chemistry molecular modeling pharmacology and clinical potential of the major classes of natural and synthetic PAF antagonists Compounds reviewed include the ginkgolides diketopiperazines neolignans hetrazepines cyclic and 1 3 dioxolan derived PAF analogs pyrrolo 1 2 c thiazoles imidazo 2 1 a isoquinolines and pyridoquinazoline carboxamides Consisting of 12 chapters written by leading experts in PAF antagonist research this book is essential reading for students researchers clinicians and medical practitioners involved in this rapidly developing field of biomedical research

*Environmental Health Perspectives*, 1993 Contains full text for issues from 1996 full text of selected articles for issues from v 2 1972

**Current Catalog** National Library of Medicine (U.S.), First multi year cumulation covers six years 1965 70

**Biochemistry of Lipids, Lipoproteins and Membranes** J.E. Vance, Dennis E. Vance, 1991-12-17 The second edition of this book on lipids lipoprotein and membrane

biochemistry has two major objectives to provide an advanced textbook for students in these areas of biochemistry and to summarise the field for scientists pursuing research in these and related fields. Since the first edition of this book was published in 1985, the emphasis on research in the area of lipid and membrane biochemistry has evolved in new directions. Consequently, this second edition has been modified to include four chapters on lipoproteins. Moreover, the other chapters have been extensively updated and revised so that additional material covering the areas of cell signalling by lipids, the assembly of lipids and proteins into membranes, and the increasing use of molecular biological techniques for research in the areas of lipid, lipoprotein, and membrane biochemistry have been included. Each chapter of the textbook is written by an expert in the field, but the chapters are not simply reviews of current literature. Rather, they are written as current, readable summaries of these areas of research, which should be readily understandable to students and researchers who have a basic knowledge of general biochemistry. The authors were selected for their abilities both as researchers and as communicators. In addition, the editors have carefully coordinated the chapters so that there is little overlap yet extensive cross referencing among chapters.

Emerging Strategies in Neuroprotection Manangos, Lal, 2013-11-21 SOLOMON H SNYDER Receptor Research Reaches Neurology Relevance to Neurodegenerative Diseases and Stroke President George Bush has heralded the 1990s as the decade of the brain, based largely on the rapid escalation of advances in the molecular neurosciences and the likelihood that these will bear therapeutic fruit before the turn of the century. There is little doubt that the 1970s and 1980s have witnessed more remarkable advances in the molecular neurosciences than all of the preceding hundred years. Identification of receptor sites for drugs and neurotransmitters, along with simple, sensitive and specific means of monitoring them, has made it possible to elucidate the mechanism of action for many known drugs and to identify new chemical entities as potential therapeutic agents. At the same time, the numbers of distinct neurotransmitters have multiplied. Prior to 1970, only the biogenic amines were well accepted as transmitters. The early 1970s witnessed the gradual acceptance of amino acids as major excitatory and inhibitory neurotransmitters. Identification of opiate receptors and the subsequent identification of the enkephalins as their endogenous ligands led to an appreciation of peptides as putative transmitters, and the accumulation of as many as a hundred neuropeptides by the decade's end. In the 1980s, the revolutions of molecular biology have been applied aggressively to the neurosciences, with molecular cloning for neuropeptide precursors, many important neurochemical enzymes, and receptors for numerous transmitters.

Reviews in Environmental Health, 1996, 1996 Organic Dusts Exposure, Effects, and Prevention Ragnar Rylander, Robert R. Jacobs, 2024-12-06 Organic dusts are particles of vegetable, animal, and microbial origin and are found in a wide range of occupational and general environments. This comprehensive handbook discusses organic dusts and their effects on man. Organic Dusts describes the different environments in which organic dusts are present; it also explains the major components of dusts and which diseases they can induce after inhalation. The first book to completely cover this important environmental exposure, this valuable reference presents a systematic approach to disease

pathology and offers revised terminology for diagnosis based on the latest information on cell reactions and the functioning of the immune system      *Biochemistry* David E. Metzler, 2001-04-25 The most comprehensive textbook reference ever to cover the chemical basis of life the Green Bible of Biochemistry has been a well respected contribution to the field for more than twenty years The complex structures that make up cells are described in detail along with the forces that hold them together and the chemical reactions that allow for recognition signaling and movement There is ample information on the human body its genome and the action of muscles eyes and the brain The complete set deals with the natural world treating the metabolism of bacteria toxins antibiotics specialized compounds made by plants photosynthesis luminescence of fireflies among many other topics The most comprehensive biochemistry text reference available on the market Organized into two volumes comprising 32 chapters and containing the latest research in the field Biological content is emphasized for example macromolecular structures and enzyme action are discussed      Platelet-activating Factor in Endotoxin and Immune Diseases Dean A. Handley, 1990      Lipid Mediators in the Immunology of Shock M. Paubert-Braquet, P. Braquet, B. Demling, R. Fletcher, M. Foegh, 2012-12-06

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