

Studying the mechanisms by which growth factors activate cellular functions has provided important insights into the normal pathways of cell growth and differentiation. Furthermore, such a study affords a basis for understanding how subversion of these pathways by defective proto-oncogenes leads to cancer. The interaction between growth factors and their appropriate receptors initiates a cascade of biochemical events during which protein phosphorylation and dephosphorylation play key roles in regulation of signal transduction and activation of effector functions. A UCLA Symposium on Cell Activation and Signal Initiation* highlighted recent progress in this area.

Transmembrane signaling via the antigen receptor on B and T lymphocytes involves polyphosphoinositide (PI) breakdown and formation of hydrolytic products that function as cellular second messengers. This mechanism is linked to a wide variety of agonist-receptor systems operating in numerous cell types and tissues. The current dogma of PI-dependent receptor signaling suggests that binding of a ligand to its specific membrane receptor results in phosphatidylinositol 4,5-bisphosphate (PIP₂) hydrolysis and formation of inositol 1,4,5-trisphosphate (IP₃) and 1,2-diacyl-glycerol (DG). The former increases intracellular Ca²⁺ concentrations, and the latter activates protein kinase C (PKC).

R. Irvine (Cambridge, UK) suggests that a third molecule, inositol 1,3,4,5-tetrakisphosphate (IP₄), promotes extracellular Ca²⁺ entry and has a synergistic effect with IP₃. Using lacrimal acinar cells, in which acetylcholine evokes sustained membrane hyperpolarization, Ca²⁺-activated K⁺ current can be evoked by intracellular perfusion of IP₄ in combination with IP₃. In this system, where hyperpolarization depends on extracellular Ca²⁺, neither IP₃ nor IP₄ is effective by itself. IP₄ also acts synergistically with IP₃ in activation of sea urchin eggs; however, the universal role of IP₄ in receptor-mediated signaling and, more specifically, in lymphoid cells has yet to be shown.

*Organized by E. Dennis, T. Hunter and M. Zenidge and held on 17-24 April 1988 in Keystone, Colorado. Abstracts have been published in the *Journal of Cellular Biochemistry*.

Cell activation and signal initiation

from Noah Isakov

Protein kinase C expression and function

Previously, PKC was thought to be a simple entity, but in the past two years it has emerged as a family of structurally related proteins that differ in tissue distribution, cofactor dependency and substrate specificity. According to data presented by U. Kikkawa (Kobe University) and K.P. Huang (NIH, Bethesda), PKC γ (following the nomenclature of L. Coussens et al. (1986) *Science* 233, 859) is distributed only in brain tissue, specifically in cerebellar and Purkinje cells, whereas PKC α and PKC β are expressed in brain as well as in peripheral tissues. PKC β is the major subtype detected by immunoblot in human leukocytes, but PKC β and low levels of PKC α are detectable in spleen extracts. Tissue staining with anti-peptide antibodies that detect variable regions unique for PKC β I and PKC β II (the result of alternative splicing of the PKC β gene) reveals that the former is distributed in granular cells in the cerebellum, and the latter occupies cells that surround Purkinje cells. All PKC subtypes are inhibited by staurosporin; they bind phorbol 12,13-dibutyrate (PDBu) with similar affinity and are activated by similar concentrations of the phorbol ester. PDBu-mediated down-regulation of PKC is relatively fast for the β subtype (within five minutes) and slow for the α subtype (three hours). Furthermore, PKC γ is degraded by trypsin within one minute, but PKC α is relatively resistant to trypsin degradation. DG and phosphatidylserine enhance PKC α degradation by trypsin, suggesting that when these cofactors bind they induce conformational changes that expose the tryptic sites.

P. Parker (Ludwig Institute, Brussels) has identified a 76 kDa molecule in an extract of resting cells that is immunoreactive with anti-PKC antibodies. Stimulation of the cells with phorbol ester results in the appearance of a 79 kDa immunoreactive molecule, suggesting post-translational modification that might also result from PKC autophosphorylation. Whether one or both forms of PKC are in an active

state remains to be tested.

A recent contribution to the growing family of kinases is that of Y. Ono (Takeda Chemical Industries, Osaka), who reported the cloning and sequencing of three additional PKC-related genes (termed δ , ϵ and ζ). The new genes are homologous to α , β and γ PKC in the C1 regulatory domain, the C3 domain and the ATP-binding site and the C4 catalytic domain. However, they lack the conserved second domain, including the pseudosubstrate sequence. The new kinases phosphorylate histone proteins at serine and threonine residues but they are much less dependent for their activation on Ca²⁺ and phospholipids, suggesting that their physiological role may differ from that of the three known PKCs.

Mixed micelle techniques that have been used to investigate cofactor specificity and stoichiometry (R.M. Bell, Duke University) support a model wherein activated PKC forms a complex with one molecule of Ca²⁺, one molecule of DG and four molecules of phosphatidylserine.

The possible role of PKC in tumorigenicity has been tested by transfection of NIH 3T3 fibroblasts with the rat brain PKC γ gene (Bell and O.J. Finn, Duke University). As a result, transfectants have altered growth *in vitro* and enhanced tumorigenicity *in vivo*. Tumors that retain transfected sequences express fewer PKC γ transcripts than the parental lines, suggesting that high level expression of PKC γ may be a factor in cell transformation, but may not be obligatory for maintaining the malignant phenotype.

A model for lipid-mediated *in vivo* regulation of PKC activity has been formulated by Bell, who finds that sphingosine and lysosphingolipids inhibit PKC activity *in vitro* and PKC-mediated functions *in vivo* in several cell types. In accordance with this model, mutations leading to enhanced sphingolipid hydrolysis or decreased sphingolipid synthesis may affect cellular PKC activity and be indirectly involved in tumor progression.

Cell Activation And Signal Initiation

Xiaolong Qi



Cell Activation And Signal Initiation :

Handbook of Cell Signaling, Three-Volume Set Ralph A. Bradshaw, Edward A. Dennis, 2003-12-02 The Handbook of Cell Signaling is a comprehensive work covering all aspects of intracellular signal processing including extra intracellular membrane receptors signal transduction gene expression translation and cellular organotypic signal responses The subject matter has been divided into five main parts each of which is headed by a recognized expert in the field Initiation Extracellular and Membrane Events Transmission Effectors and Cytosolic Events Nuclear Responses Gene Expression and Translation Events in Intracellular Compartments Cell Cell and Cell Matrix Interactions Covered in extensive detail these areas will appeal to a broad cross disciplinary audience interested in the structure biochemistry molecular biology and pathology of cellular effectors Tabular and well illustrated the Handbook will serve as an in depth reference for this complex and evolving field Tabular and well illustrated the Handbook will serve as an in depth reference for this complex and evolving field Contains approximately 470 articles Provides well organized sections on each essential area in signaling Includes discussion on everything from ligand receptor interactions to organ organism responses Extremely user friendly **Cellular and Molecular Immunology E-Book** Abul K. Abbas, Andrew H. Lichtman, Shiv Pillai, 2014-08-15 Popular for its highly visual straightforward approach Cellular and Molecular Immunology delivers an accessible yet thorough understanding of this active and fast changing field Drs Abul K Abbas Andrew H Lichtman and Shiv Pillai present key updates in this new edition to cover the latest developments in antigen receptors and signal transduction in immune cells mucosal and skin immunity cytokines leukocyte endothelial interaction and more With additional online features this is an ideal resource for medical graduate and undergraduate students of immunology who need a clear introductory text for immunology courses Consult this title on your favorite e reader conduct rapid searches and adjust font sizes for optimal readability Develop a thorough clinically relevant understanding of immunology through a clear overview of immunology with a distinct focus on the management of human disease Visualize immunologic processes more effectively Meticulously developed and updated illustrations 3 dimensional art and all new animations provide a detailed visual description of the key immunologic and molecular processes Grasp the details of experimental observations that form the basis for the science of immunology at the molecular cellular and whole organism levels and draw the appropriate conclusions Find information more quickly and easily through an organized chapter structure and a more logical flow of material Glean all essential up to date need to know information about immunology and molecular biology through extensive updates that cover cytokines innate immunity leukocyte endothelial interactions signaling costimulation and more Benefit from numerous new figures and tables that facilitate easier retention of the material quick summaries of each chapter and nearly 400 illustrations that clarify key concepts **Wintrobe's Clinical Hematology** Daniel A. Arber, Bertil Glader, Alan F. List, Robert T. Means, Frixos Paraskevas, George M. Rodgers, 2013-08-29 With the 13th edition Wintrobe s Clinical Hematology once again bridges the gap

between the clinical practice of hematology and the basic foundations of science Broken down into eight parts this book provides readers with a comprehensive overview of Laboratory Hematology The Normal Hematologic System Transfusion Medicine Disorders of Red Cells Hemostasis and Coagulation Benign Disorders of Leukocytes The Spleen and or Immunoglobulins Hematologic Malignancies and Transplantation Within these sections there is a heavy focus on the morphological exam of the peripheral blood smear bone marrow lymph nodes and other tissues With the knowledge about gene therapy and immunotherapy expanding new up to date information about the process and application of these therapies is included Likewise the editors have completely revised material on stem cell transplantation in regards to both malignant and benign disorders graft versus host disease and the importance of long term follow up of transplantation survivors

Cellular and Molecular Immunology: First South Asia Edition-E-Book Abul K. Abbas, Andrew H Lichtman, Shiv Pillai, 2017-08-02 The top required and recommended immunology text worldwide Cellular and Molecular Immunology by Drs Abul K Abbas Andrew H H Lichtman and Shiv Pillai is a clear well written and superbly illustrated introduction to the field The First South Asia Edition retains a practical clinical focus while updating and revising all content to ensure clarity and comprehension bringing readers fully up to date with new and emerging information in this challenging area Highlights the implications of immunologic science for the management of human disease emphasizing clinical relevance throughout Provides a highly visual full color description of the key immunologic and molecular processes with a fully updated comprehensive and consistent art program Helps readers grasp the details of experimental observations that form the basis for the science of immunology at the molecular cellular and whole organism levels and draw the appropriate conclusions Includes summary boxes that assist with rapid review and mastery of key material [Encyclopedia of Immunobiology](#), 2016-04-27 Encyclopedia of Immunobiology Five Volume Set provides the largest integrated source of immunological knowledge currently available It consists of broad ranging validated summaries on all of the major topics in the field as written by a team of leading experts The large number of topics covered is relevant to a wide range of scientists working on experimental and clinical immunology microbiology biochemistry genetics veterinary science physiology and hematology The book is built in thematic sections that allow readers to rapidly navigate around related content Specific sections focus on basic applied and clinical immunology The structure of each section helps readers from a range of backgrounds gain important understanding of the subject Contains tables pictures and multimedia features that enhance the learning process In depth coverage allows readers from a range of backgrounds to benefit from the material Provides handy cross referencing between articles to improve readability including easy access from portable devices **Fundamental Immunology** William E. Paul, 2012-12-03 This standard setting textbook has defined the field of immunology since 1984 and is now in its Seventh Edition continuing to deliver the detailed authoritative and timely coverage readers expect This comprehensive up to date text is ideal for graduate students post doctoral fellows basic and clinical immunologists microbiologists and infectious

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The Role of EIF3 in Translation Initiation in T Lymphocytes Purvi Patel,2004

Selective Initiation and Control of Antibody Responses by Dendritic Cell and B Cell Mediated ICOS Signaling Kevin Scott Larimore,2007

Clinical and Laboratory Evaluation of Human Autoimmune Diseases Robert M. Nakamura,David F. Keren,David J. Bylund,2002 Eminently practical with up to date information this exciting new book explores the limitations and usefulness of various clinical laboratory tests for the diagnosis and evaluation of human autoimmune diseases The editors provide clinical immunological laboratories with an invaluable aid for their day to day problems and consultative interaction with clinicians

Studia biophysica ,1990

DNA and Cell Biology ,2002

Jawetz Melnick & Adelbergs Medical Microbiology 28 E Stefan Riedel,Stephen A. Morse,Timothy A. Mietzner,Steve Miller,2019-08-25 Understand the clinically relevant aspects of microbiology with this student acclaimed full color review bolstered by case studies and hundreds of USMLE style review questions A Doody s Core Title for 2024 2021 Since 1954 Jawetz Melnick Adelberg s Medical Microbiology has been hailed by students instructors and clinicians as the single best resource for understanding the roles microorganisms play in human health and illness Concise and fully up to date this trusted classic links fundamental

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Signal Transduction in Cytoplasmic Organization and Cell Motility Peter Satir,John S. Condeelis,Elias Lazarides,1988

The Journal of Immunology ,2008 **Current Topics in Microbiology and Immunology** ,1967 Cell Signaling and Growth Factors in Development Klaus Unsicker,Kerstin Krieglstein,2006 Combining a comprehensive treatment of both embryogenesis and organ development in one reference work this handbook is structured according to organ systems It addresses the functions of all signaling pathways and growth factors important for the development of the embryo and the adult With its focus on vertebrates this volume provides an overview of the molecular communication regulating such processes as cell division migration and differentiation Additionally sections on developmental disorders and related novel therapeutic strategies highlight applications in molecular medicine *Kidney Transplantation* Peter J. Morris,2001 This fifth edition of KIDNEY TRANSPLANTATION remains the most comprehensive and definitive text on all aspects of renal transplantation as well as the psychological and ethical issues involved Almost every chapter has been revised or rewritten by new authors to incorporate the most essential and up to date information *The Cancer Handbook, 2 Volume Set* Malcolm Alison,2007-07-30 The Cancer Handbook provides a comprehensive overview of scientific and clinical information in cancer research and medicine oncology This area is one of the most intensively studied in biology and medicine resulting in a huge amount of new information being published every year This book summarizes and explains key facts and recent developments It is aimed at a wide variety of readers who need easy access to knowledge concerning all major aspects of cancer biology without too much clinical detail or specialist research material The Cancer Handbook stands out from existing oncology textbooks and reference works in that it bridges the gap between the molecular biology of cancer and clinical diagnosis and treatment As more and more laboratory research is applied to clinical management e g the use of monoclonal antibodies as drugs it is important that clinicians understand the aetiology of the disease and the molecular basis of the new therapeutic approaches It is also important for laboratory scientists to appreciate the potential applications of their research

and the practical issues involved in translating it to clinical practice For this second edition all the sections have been fully revised and updated with new chapters addressing important topics that have gained prominence in recent years New editors and authors have brought additional expertise to the project For example in the section on the Molecular and Cellular Basis of Cancer there are new chapters on stem cells epigenetics and microRNAs as well as chapters on the links between cancer and development and inflammation In the Treatment section the emphasis is now on multidisciplinary team management of different cancers plus there are new chapters on clinical trial design RNA interference and rational drug design The page design and the quality of the diagrams has been improved with all illustrations now in full colour The glossary has been made more informative and easy to use

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