

L. Wolff and A.S. Perkins (Eds.)

Molecular Aspects of Myeloid Stem Cell Development



Springer

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Anthony J. Pawson



Molecular Aspects Of Myeloid Stem Cell Development:

Molecular Aspects of Myeloid Stem Cell Development Linda Wolff, Archibald S. Perkins, 2012-12-06 A workshop on MOLECULAR ASPECTS OF MYELOID STEM CELL DEVELOPMENT was held at the Historic Inns in Annapolis MD during April 30 May 3 with approximately 70 persons attending. The enormous success of this meeting was attributable to the recent outburst of information generated from two areas of study: transcriptional regulation of developmentally important myeloid genes and molecular dissection of chromosomal abnormalities in human myeloid leukemias. It was reassuring that studies of normal myelopoiesis and abnormal myelopoiesis as observed in dysplasias and neoplasia are revealing several interrelated mechanisms of gene regulation. However, great challenges await us as we try to determine how these and other mechanisms in this intricate system orchestrate the ultimate fate of cells, e.g., proliferation, differentiation, or apoptosis. This volume of *Current Topics in Microbiology* encapsulates many of the key aspects of the workshop, summarizing research over the past few years on the ontogeny and pathology of myeloid cells. Investigations into the complex process of normal myeloid cell maturation were first made possible through development of *in vitro* clonogenic assays. These established the relationships of colony stimulating factors, interleukins, and their combinations to the specific fates of myeloid progenitors derived from the bone marrow and spleen. Molecular studies became feasible, however, through the later establishment of several cell culture systems involving immortalized cells which, under the proper induction, could fairly accurately recapitulate the myelopoietic process.

Specificity, Function, and Development of NK Cells Klas Kärre, Marco Colonna, 2012-12-06 Our understanding of the function of natural killer (NK) cells has dramatically changed in recent years. The discovery of NK receptors specific for MHC class I molecules and the study of the role of co-stimulatory and adhesion molecules have led to an understanding of how NK cells recognize tumor and virally infected cells that have lost expression of MHC class I molecules or have altered distribution of normal cell surface molecules. Such recognition events lead to intracellular signals which can be either stimulatory or inhibitory. This book provides an insight into how NK cells develop, how they learn to distinguish altered cells from normal cells, and into their biological role in controlling infections and tumors.

Morphogenesis and Maturation of Retroviruses Hans-Georg Kräusslich, 2012-12-06 Retroviruses arguably belong to the most fascinating of all viruses because of their unusual and highly efficient mode of replication involving reverse transcription and integration of the viral genome and a complex system of transcriptional and post-transcriptional regulatory mechanisms. The importance of retroviruses as human and animal pathogens has also enhanced scientific and medical interest in this diverse group of viruses and has spurred an intensive search for novel and improved antiviral agents. More recently, analysis of retroviral replication and, in particular, understanding the formation and composition of the virus particle has received additional attention because of the promise of retroviral vectors as vehicles for human somatic gene therapy. Many recent advances have been made in our understanding of the molecular mechanisms governing assembly and release.

of infectious retrovirus particles This book attempts to summarize these recent developments and to provide an overview of our current knowledge on retrovirus particle formation The individual chapters of the book deal with specific steps in the pathway of retroviral morphogenesis and maturation starting at the time when the components of the virus have been synthesized within the infected cell and ending once the infectious virion has been released from the cell An introductory chapter provides a comparative description of the structure and morphology of various retroviruses

Attempts to Understand Metastasis Formation I Ursula Günthert, Walter Birchmeier, 2012-12-06 In metastasis tumor cells disseminate from the primary lesion and home to secondary organs where they may remain dormant for a long time Metastasis formation is still the most feared manifestation for tumor patients and clinicians Although improvements have been made concerning earlier detection and specific therapy most of the cancer patients still die of distant metastases The purpose of these three volumes is to review the recent progress in molecular metastasis research and to attempt to further understand the biology of this multifocal process With respect to present day molecular biology the pioneers of metastasis research established the basic concepts of metastasis formation in the 1970s and 1980s namely clonal selection of metastatic cells heterogeneity of metastatic subpopulations organ specificity of metastasis and the importance of angiogenesis Fidler Kripke Nicolson Folkman and others In the 1980s and 1990s several of the molecules involved were identified and their network interactions elucidated These three volumes of Current Topics in Microbiology and Immunology compile the most recent developments on these metastasis related molecules their interactions regulation and ways to interfere with their action It became evident that metastasis related molecules are confined to distinct cellular compartments such as the extracellular space the cell membrane the cytoplasmic signalling network and the nuclear regulatory system For the complex metastatic cascade proteolysis and alterations in adhesive functions are the most obvious and thus one of the most thoroughly investigated processes

Origin and Evolution of the Vertebrate Immune System L. Du Pasquier, G.W. Litman, 2012-12-06 The comparative approach to immunology can be traced to the era of Pasteur and Metchnikov in which observations regarding foreign recognition in invertebrates was a factor in the development of the principal concepts that created the foundation of what now is the broad field of immunology With each major experimental and conceptual breakthrough the classical albeit essential question has been asked are the immune systems of phylogenetically primitive vertebrates and invertebrates similar to that of mammals Somewhat surprisingly for the jawed vertebrates the general answer has been a qualified form of yes whereas for agnathans and invertebrate phyla it has been no so far The apparent abruptness in the appearance of the immune system of vertebrates is linked to the introduction of the somatic generation of the diversity of its antigen specific receptors Therefore the questions regarding the origin and evolution of the specific immune system revolve around this phenomenon With respect to the origin of the system aside from the origin of the rearranging machinery itself the study of which is still in its infancy one can ask questions about the cellular and molecular contexts in which the mechanism was

introduced Immunobiology of Bacterial CpG-DNA H. Wagner,2012-12-06 Bacterial CpG DNA sequences not only serve for genetic information but act as danger signal to alert immune cells such as macrophages and dendritic cells CpG DNA directly causes activation of these members of the innate immune system yielding in up regulation of co stimulatory molecules and pro inflammatory cytokines As such they act as natural adjuvants to promote protective Th1 polarized T cell immune responses This book is the first comprehensive review of the data emerging in this field Antigen Presentation J. Lindsay Whitton,2013-03-07 Antigen presentation is central to the immune response and is instrumental in ensuring that the response mounted is that best suited to the eradication of the particular microbe faced In this volume experts in the field provide state of the art descriptions of the antigen presentation pathways How do viruses disrupt these critical pathways and to what effect Do all tissues present antigen in the same way If not why What are the consequences of dysfunctional antigen presentation seen in certain genetic disorders This book considers not only the molecular details but also their relevance to the whole organism Blood Cell Biochemistry Anthony D. Whetton,John Gordon,1996-08-31 Historically the field of hematopoietic growth factor research began with the work of Carnot and Deflandre in 1906 they suggested that the rate of erythropoiesis is regulated by a humoral factor found in the blood namely erythropoietin From this comparatively early start accelerating progress has been made in erythropoietin research which demonstrates the general trends in this field of study Erythropoietin was purified to homogeneity by 1977 from enormous quantities of urine from aplastic anemia patients Subsequently the gene for erythropoietin has been cloned 1985 and massive quantities of this growth factor have been produced for clinical trials late 1980s onward Erythropoietin has become established as a pharmaceutical product of great value in the treatment of a number of diseases most notably chronic renal failure Once the ligand had been cloned interest turned to the erythropoietin receptor which was cloned in 1989 Since then structure function studies have been performed on receptor mutants cellular signaling events downstream from the occupied receptor have been identified and the specific producer cell types and molecular stimuli for erythropoietin production have been thoroughly investigated as has the regulation of erythropoietin gene transcription This schedule of events since the 1970s typifies that seen for a number of hematopoietic growth factors Along the way the hematopoietic growth factors have been recognized as members of the cytokine family of signaling molecules that are important in a number of different physiological and pathological situations see below **Genetic Instability and Tumorigenesis** Michael B. Kastan,2012-12-06 M B KASTAN Cancer is a disease resulting from alterations of cellular genes which cause phenotypic changes in somatic cells Usually when we think about genetic diseases we think about inheriting one or two abnormal genes from our parents and these gene abnormalities confer the disease phenotype In contrast in the majority of cancers no such inherited gene abnormalities can be identified which does not mean that they do not exist and there is no obvious family history suggesting an inherited disease The vast majority of genes which are altered in the cancer cells are not transmitted through the germ line but rather become abnormal in

somatic cells sometime during the lifetime of the individual Thus the critical question which arises is how do these genetic changes occur in somatic cells Epidemiologic data suggest that exposure to environmental carcinogens contribute to the genesis of at least 80% of all human cancers DOLL and PETO 1981 Thus it is natural to suspect that the genetic changes in somatic cells which contribute to the transformed phenotype arise from DNA damage caused by such exposures Therefore understanding how cells respond to DNA damaging agents is likely to be an important component of our understanding of the genesis of human tumors

Protein Modules in Signal Transduction Anthony J. Pawson, 2012-12-06 This volume in the series Current Topics in Microbiology and Immunology focuses on protein modules in signal transduction Topics covered include functions of SH2 and SH3 domains structure and function of LIM domains and the IRS signalling system

Vascular Growth Factors and Angiogenesis Lena Claesson-Welsh, 2012-12-06 Currently the cellular and molecular mechanisms governing the development and regulation of the vasculature are studied intensely and the field is rapidly progressing Recently novel growth factors and growth factor receptors specifically acting on endothelial cells have been discovered Through these factors communication networks are established between endothelial cells the basement membrane and the pericytes this interplay is critical for the regulated development and maintenance of the vasculature The awareness that deregulated angiogenesis contributes to the progression of a number of diseases such as cancer and inflammatory diseases has clearly spurred the field to move forward The focus of this book is on two important classes of endothelial cell specific growth factors the vascular endothelial growth factor VEGF family and the angiopoietins and on their mechanisms of action The reader will find up to date focused reviews which give the current picture and indicate future directions I would like to honor Dr Judah Folkman for his important contributions to the establishment of the field and thank him for his support Lena Claesson Welsh List of Contents N FERRARA Vascular Endothelial Growth Factor Molecular and Biological Aspects M G PERSICO V VINCENTI and T DIPALMA Structure Expression and Receptor Binding Properties of Placenta Growth Factor PIGF 31 U ERIKSSON and K ALITALO Structure Expression and Receptor Binding Properties of Novel Vascular Endothelial Growth Factors 41 M SHIBUYA N ITO and L CLAEISSON WELSH Structure and Function of Vascular Endothelial Growth Factor Receptor 1 and 2 59 J TAIPALE T MAKINEN E ARIGHI E

Combinatorial Chemistry in Biology Michael Famulok, Ernst-L. Winnacker, Chi-Huey Wong, 2013-06-29 The essence of combinatorial chemistry or techniques involving molecular diversity is to generate enormous populations of molecules and to exploit appropriate screening techniques to isolate active components contained in these libraries This idea has been the focus of research both in academia and in the pharmaceutical or biotechnology industry Its developments go hand in hand with an exploding number of potential drug targets emerging from genomics and proteomics research When the editors of Current Topics in Microbiology and Immunology encouraged us to assemble the present volume on Combinatorial Chemistry in Biology we immediately felt that this might prove quite beneficial for the audience of this series The field of combinatorial chemistry extends over a broad

range of disciplines from synthetic organic chemistry to biochemistry from material sciences to cell biology Each of these fields may have its own view on this topic something which is reflected in a growing number of monographs and special editions of journals devoted to this issue or aspects thereof The title of the present volume of Springer Verlag's series suggests that it also has its own special focus And generally speaking this is not wrong we would even claim the special focus of this volume is on the immunologically relevant aspects of combinatorial chemistry

Immunoreceptor Tyrosine-based Inhibition Motifs Marc Daeron, Eric Vivier, 2012-12-06 Novel molecular motifs named Immunoreceptor Tyrosine based Inhibition Motifs ITIMs have recently been recognized in the intracytoplasmic domains of a still increasing number of receptors which control cell activation and proliferation Research on ITIM bearing molecules has developed exponentially during the last three years generating new concepts with important consequences in basic research and with exciting potential clinical applications The present volume contains 15 reviews written by authors who all made significant contributions to the identification of ITIM bearing molecules and the study of their biological properties It constitutes the first synthesis ever published that is specifically devoted to this emerging topic

Toxoplasma gondii Uwe Gross, 2012-12-06 For years toxoplasmosis has been known as disease mostly affecting newborns Since immunocompromised patients AIDS present a high risk of reactivation of chronic toxoplasmosis this parasitic disease has gained increasing interest Besides presenting clinical and therapeutical concepts this volume provides current knowledge about genetics and immunology of *T. gondii* and the interaction with its host Since in vivo and in vitro models of toxoplasmosis exist and genetic manipulation has become possible this protozoan parasite has recently been accepted as a model for understanding the pathogenesis and persistence of other intracellular parasites The articles of the book comprise both reviewing current concepts and reporting on yet unpublished results of leading scientists in this field

Adeno-Associated Virus (AAV) Vectors in Gene Therapy Kenneth I. Berns, Catherine Giraud, 2012-12-06 Human gene therapy holds great promise for the cure of many genetic diseases In order to achieve such a cure there are two requirements First the affected gene must be cloned its sequence determined and its regulation adequately characterized Second a suitable vector for the delivery of a good copy of the affected gene must be available For a vector to be of use several attributes are highly desirable these include ability to carry the intact gene although this may be either the genomic or the cDNA form in a stable form ability to introduce the gene into the desired cell type ability to express the introduced gene in an appropriately regulated manner for an extended period of time and a lack of toxicity for the recipient Also of concern is the frequency of cell transformation and in some cases the ability to introduce the gene into nondividing stem cells Several animal viruses have been tested as potential vectors but none has proven to have all the desired properties described above For example retroviruses are difficult to propagate in sufficient titers do not integrate into nondividing cells and are of concern because of their oncogenic properties in some hosts and because they integrate at many sites in the genome and thus are potentially insertional mutagens Additionally genes

introduced by retroviral vectors are frequently expressed for relatively short periods of time A second virus used as a vector in model systems has been adenovirus Ad [Biomedical Index to PHS-supported Research: pt. A. Subject access A-H](#) ,1992

Attempts to Understand Metastasis Formation II Ursula Günthert,Walter Birchmeier,2012-12-06 Within the last decade the molecular biology of tumor models has revealed the identification of several metastasis related molecules These volumes attempt to review the most recent approaches of their mechanisms regulation and way to treat their malignant alterations The first volume covers the presentation of proteases and inhibitors and their role in invasion of tumor cells also cell adhesion molecules and their interaction with the extracellular matrix In the second volume the regulation of tumor progression and angiogenesis by cytokines growth factors and motility factors is outlined The third volume deals with detection of micrometastases and therapeutic approaches such as immunotherapy gene therapy chemotherapy and surgical strategies to combat metastatic spread

Pathology of Septic Shock Ernst T. Rietschel,Hermann Wagner,2012-12-06 Severe sepsis and septic shock are the most serious complications of bacterial infections Both gram positive and gram negative bacteria can trigger these extreme inflammatory responses and by so doing cause substantial morbidity and mortality In the United States alone over 400 000 patients suffer from septicaemia each year and approximately 100 000 of these patients die despite optimal intensive care and modern antimicrobial therapy These dramatic figures have prompted intensive research to define the bacterial and host factors involved in the septic response Scientists from many disciplines including chemistry physics biology medical microbiology immunology and pharmacology have worked closely with clinicians to achieve rapid and profound progress To translate this newly acquired knowledge into clinical practice clinical trials have also been performed to evaluate numerous new therapeutic drugs The disappointing results from these trials have underscored a major lesson namely that sepsis constitutes an extremely complex syndrome and that basic and clinical research must be greatly intensified in order to illuminate its molecular mechanisms At this stage the editors of the present volume of Current Topics in Microbiology and Immunology considered it would be rewarding to compile a volume summarizing our present basic and clinical knowledge on sepsis Our particular gratitude extends to those international experts who have followed our invitation and elaborated on particular areas of the basic and clinical aspects of this field

Bacterial Infection: Close Encounters at the Host Pathogen Interface Peter K. Vogt,Michael J. Mahan,2012-12-06 When it comes to bacterial disease we are living in a state of false security Antibiotics have indeed brought unprecedented health benefits protection from and cure of bacterial diseases during the past 50 years But there are ominous signs that the fortress and the defenses built on antibiotics are crumbling They are crumbling because we wittingly or unwittingly created selective conditions for the emergence of superior pathogens that can no longer be controlled by antibiotics There are numerous warnings After a long period of eclipse tuberculosis has now emerged as a serious threat unchecked by antibiotic treatment Recent years have seen reports of cholera epidemics of anthrax infections of serious problems with Salmonella and

even with E coli just to name a few Mankind is in a race with microbial invaders The challenge is to anticipate and respond to developments that affect the precarious balance between man and microbe This will require new knowledge and it will take time for an effective application of that knowledge

The Coxsackie B Viruses Steven Tracy, Nora M. Chapman, Brian W.J. Mahy, 2013-06-29

Late in the 1940s a virus was isolated from a young patient with a flaccid paralysis in the sleepy Hudson River town of Coxsackie in the state of New York Within the next few years it was apparent that this and other similar viruses were not polioviruses but were indeed a new group of viruses that by the mid 1950s had been found to be commonly associated with pediatric inflammatory heart disease Two groups of coxsackieviruses A and B were differentiated on the basis of the type of paralysis induced in suckling mice by these viruses Group B coxsackieviruses because of their primacy as etiologic agents of human acute viral myocarditis and its relatively common sequela dilated cardiomyopathy are the focus of this volume of the century approaches the massive international effort to eradicate polioviruses through vaccination as causes of human disease has been successful in the Western Hemisphere and in many parts of Europe and it is expected that worldwide eradication may be achieved within the near future While this is wonderful news there are sadly no similar efforts being planned to combat the numerous other human enteroviruses that daily incur widespread morbidity and mortality throughout the world While this is due in part to the lack of specific knowledge about the other human enteroviruses it is also due to the perceptions of industry that there is insufficient profit to be made by developing these vaccines

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