

# 141 Current Topics in Microbiology and Immunology

## **Mechanisms in B-Cell Neoplasia 1988**

Edited by  
M. Potter and F. Melchers



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# Mechanisms In B Cell Neoplasia 1988 Workshop At The National Cancer Institute

**Michael Potter, Fritz Melchers**



## **Mechanisms In B Cell Neoplasia 1988 Workshop At The National Cancer Institute:**

**Mechanisms in B-cell Neoplasia 1988** Fritz Melchers, Michael Potter, 1988      **Mechanisms in B-Cell Neoplasia 1988** Michael Potter, Fritz Melchers, 2013-03-07 The papers in this book were presented at the 6th Workshop on Mechanisms in B Cell Neoplasia held in Bethesda March 23 25 1988 On alternate years this meeting is sponsored by the Basel Institute of Immunology in Basel Switzerland and by the National Cancer Institute in Bethesda and is attended by 100 to 150 participants This 6th workshop like the preceding five was characterized by intense and enthusiastic discussion which reflects we think the exciting growth and development of this field It is quite clear however that despite many general advances an understanding of the precise underlying mechanisms in B cell tumor development is not yet defined Probably there is no single mechanism for all the various forms of B cell neoplastic development Many different forms of B cell neoplasms are known and these are distinguished by several characteristics 1 the stage of development attained by the tumor stem cells 2 mode of growth slow or fast 3 association with natural or inductive etiologic agents and 4 specific and consistent mutational mechanisms such as retroviral insertion chromosomal rearrangement Those characteristic forms which arise naturally in relatively high frequency or those tumors with hallmark properties which can be induced consistently are the models most frequently studied e g endemic Burkitt's lymphoma follicular lymphoma acute and chronic lymphocytic leukemia and multiple myeloma in man bursal lymphoma in chickens Abelson virus induced pre B cell lymphomas and plasmacytomas in mice and immunocytomas in rats Each model system has special problems and advantages      *Mechanisms in B-Cell Neoplasia 1992* Michael Potter, Fritz Melchers, 2013-03-08 Main topics covered B Cell Development Immunoglobulin Gene Rearrangement Multiple Myeloma Plasmacytomas Lymphomas B CLL Follicular Lymphomas BCL 2 BCL 1 Lymphomas EBV AIDS Associated Lymphomas Oncogenes and Transcriptional Factors text to follow      *National Library of Medicine Current Catalog* National Library of Medicine (U.S.), 1993 First multi year cumulation covers six years 1965 70      **Mechanisms in B-cell Neoplasia 1990** Michael Potter, Fritz Melchers, 1990      Retroviral Insertion and Oncogene Activation Hsing-Jien Kung, Peter K. Vogt, 2012-12-06 An integrated retrovirus effectively becomes part of the cellular genome but with the difference that the virus to a large extent retains control over its own expression through nontranslated sequences in the long terminal repeat LTR Some retroviruses also code for nonstructural proteins that further regulate proviral expression Integration changes the cell genome it adds viral genes and in the case of transducing retroviruses also adds cell derived oncogenes that have been incorporated into the viral genome Integration can also have consequences for cellular genes The transcriptional signals in a provirus can activate expression of neighboring cellular genes the integration even can disrupt and thus inactivate cellular genes These effects of retroviral genomes take place in cis they are referred to as insertional mutagenesis and are the subject of this volume Almost 10 years have passed since W Hayward S Astrin and their colleagues found that in B cell lymphomas of chickens induced by avian leukosis virus transcription of the cellular proto oncogene myc

was upregulated through the integration of a complete or partial provirus in its vicinity This landmark discovery suggested a mechanism by which retro viruses that do not carry cellular oncogenes in their genome nonacute retroviruses can cause cancer It contributed the first evidence for the carcinogen potential of oncogenes that are not part of a viral genome

**Pathogenesis of Shigellosis** P.J. Sansonetti,2012-12-06 Shigellosis is present all over the world Anyone traveling in developing countries knows that the control of this invasive disease of the intestine is a priority task for physicians and public health authorities Victims are essentially young children and complications such as the hemolytic uremic syndrome make shigellosis a systemic disease rather than simply an infection of the colonic mucosa However Westerners should not consider shigellosis as an unlikely threat of the tropics The disease arises in industrialized countries as soon as breaches in sanitation appear A few months ago at least 500 people developed shigellosis in northern France in an outbreak of *Shigella sonnei* infection due to accidental contamination of an urban water delivery system The pathogenesis of shigellosis is an extraordinary topic of research because study of the invasion of the colonic mucosa addresses fundamental questions on the molecular and cellular mechanisms by which a bacterial pathogen can penetrate non phagocytic cells survive multiply spread in the intracellular compartment and eventually kill host cells Further development of the infection within subepithelial tissues as well as the mechanisms that contribute to the eradication of this process have barely been studied

**ADP-Ribosylating Toxins** Klaus Aktories,2012-12-06 ADP ribosylating toxins have been the focus of intensive research for more than 30 years Researchers from diverse fields of science have taken an interest in these bacterial toxins they are studied for example by microbiologists biochemists cell biologists and pharmacologists There are two principal reasons for the broad and still growing interest in ADP ribosylating toxins First insights into the structure and functions of the toxins might be the key to prevention and treatment of diseases caused by the toxin producing infectious micro organisms Second the ADP ribosylating toxins provide potent and often unique pharmacological tools for the study of the physiological functions of their target proteins The latter is especially the case with cholera and pertussis toxins which both modify the IX subunits of heterotrimeric G proteins involved in signal transduction pathways These toxins have proved invaluable in extending our basic understanding of the regulation of hormone controlled signal transduction This volume provides a review and an update of recent studies on the basic properties of bacterial ADP ribosylating toxins and or exoenzymes Our current knowledge of the cellular entry mechanisms of ADP ribosylating toxins is reviewed by MADSHUS and STENMARK WILSON and COLLIER then deal with recent insights into the enzyme mechanism and active site structure of diphtheria toxin and *Pseudomonas aeruginosa* exotoxin A which modify elongation factor 2 Toxins which ADP ribosylate heterotrimeric G proteins involved in transmembrane signal transduction are the subject of the next two chapters **Function and Specificity of**

**γ/δ T Cells** Klaus Pfeffer,Klaus Heeg,Hermann Wagner,Gert Riethmüller,2012-12-06 Our current understanding of a T cell receptor TCR expressing T cells advanced from function and specificity to the molecular organization of the TCR We now

know that the TCR  $\alpha$  and chains together express specificity for antigenic peptides presented by the responder MHC allele thus explaining the phenomenon of MHC restriction at a molecular level Surprisingly even though our perception of the molecular organization of the  $\gamma\delta$  TCR is well advanced current knowledge of function and specificity of the  $\gamma\delta$  T cell subset is poor Therefore it appeared rather timely to bring together scientists pioneering research on  $\gamma\delta$  T cells for the International Workshop on Function and Specificity of  $\gamma\delta$  T cells held October 11-14 1990 at Schloss Elmau Bavaria FRG Besides offering a scientific forum for open discussions it was also hoped that such a workshop would be seminal for collaborative interactions and personal relationships among scientists addicted to  $\gamma\delta$  T cells

**The Role of Viruses and the Immune System in Diabetes Mellitus** Thomas Dyrberg, 2013-06-29 Research in diabetes has accelerated in two areas both of which are being reviewed in CTMI The first is the use of a variety of animal models the second is basic research in human investigation islet cell antigens and mapping of genes associated with susceptibility to disease Dr Thomas Dyrberg accepted editorial responsibility for this volume which covers the first area A second book to be published later in the year is edited by Drs Brekkeskov and Hansen CTMI 164 see page VI for contents Although the contributors to both volumes represent the international scientific community the editors are from the Hagedorn Research Laboratory in Denmark Work at this institute and the Steno Memorial Hospital has been dedicated to research in diabetes for decades and the institutions were appointed WHO Collaborating Centres for Research and Training on the Pathogenesis of Diabetes Mellitus in 1983 It is worth noting that while addressing the hypothesis of the role of class II major histocompatibility glycoproteins in autoimmune diabetes insulin dependent diabetes IDDM a number of investigators established animal models in which class II molecules were expressed under the control of the rat insulin promoter While generating interesting information on IDDM the finding of immunologic tolerance in such transgenic mice has attracted the attention of several basic immunologic laboratories for quite different reasons Thus we are reminded again of the Pasteur dictum that chance favors the prepared mind Michael B A Oldstone M D

**Membrane Defenses Against Attack by Complement and Perforins** Charles J. Parker, 2012-12-06 In this volume a comprehensive review of membrane proteins that regulate complement and perforin mediated cytotoxicity is presented A detailed analysis provided of the biochemical molecular and functional features of these proteins the glycosyl phosphatidylinositol linked proteins are covered with emphasis placed on the functional importance of this type of membrane anchor Further chapters include reviews of the effects of complement activation on cells that are metabolically active and of the regulation of cell killing by cytotoxic lymphocytes considering the similarities and disparities between the complement and perforin systems The therapeutic use of recombinant CR1 for immune mediated pathophysiological processes is discussed in a separate section

**Adhesion in Leukocyte Homing and Differentiation** Dominique Dunon, Charles R. Mackay, Beat A. Imhof, 2012-12-06 This volume of Current Topics in Microbiology and Immunology was planned in parallel with an EMBO workshop on cell cell Interactions in Leukocyte Homing and Differentiation held at the Basel Institute for

Immunology in November 1992 and many of the workshop speakers have contributed to it Cell adhesion is one of the most dynamic fields of biological research and presented in this book is the current knowledge on the structure and function of the major families of cell adhesion molecules the integrins the selectins the immunoglobulin superfamily and CD44 Complex interactions between the members of these families mediate diverse adhesion functions including leukocyte leukocyte interactions lymphocyte homing inflammation and lymphocyte stromal cell interaction during hematopoiesis A great deal of emphasis is placed on the regulatory elements that control the expression and function of adhesion molecules Cytokines not only induce the expression of certain adhesion molecules but may also modify their functional status For instance the integrins exist in either an inactive nonfunctional form or an active functional form and a number of intracellular or extracellular stimuli modify integrin function This is particularly important during leukocyte binding to endothelium and transendothelial migration which proceeds through a cascade of adhesion events Although cell adhesion molecules play an important role in many processes this book concentrates on their role within the immune system A number of chapters discuss the migration of lymphocytes between hematopoietic organs such as the thymus lymph nodes Peyer s patches and spleen

**Retroviruses** Ronald Swanstrom, Peter K. Vogt, 2012-12-06 This book gives a synthesis of current knowledge on retrovirology Each chapter deals with a different step in the virus life cycle detailing the molecular aspects of virus replication The comparison of different retroviruses exemplifies variations Specific topics include the evolution of retrovirus genomes integration of the provirus viral DNA transcriptional and translational control of viral gene expression processing of viral proteins and packaging of virion RNA Data on HIV and HTLV 1 are covered as well as research on animal retrovirus systems

**Hepadnaviruses** William S. Mason, Christoph Seeger, 2012-12-06 Pioneering work on hepatitis B virus and hepatitis delta virus and the discovery of hepatitis B like virus in animals during the 1970 s has been followed over the past ten years by an explosion of interest in how these viruses replicate maintain chronic infections and cause liver disease and hepatocellular carcinoma The purpose of this book is two fold First the authors of each chapter provide a summary of their specialty that will not only serve as an introduction but will also provide the newcomer to hepatitis B virology with up to date information and insights into the goals and accomplishments of each area of investigation Second since the diversification of interests and increased specialization of hepadnaviruses researchers has reached a level where it is no longer possible for any one individual to read all the primary literature this book will help to refocus interest on what is after all the major objective to understand and ultimately treat or prevent chronic liver disease and liver cancer Accordingly chapters are included which span a range of interests from the management of hepatitis B patients to new approaches to antiviral therapy from the role of hepadnavirus gene expression in DNA replication to the role of ribozymes in the delta virus life cycle from liver cancer in naturally infected woodchucks to liver disease in HBV transgenic mice to the use of hepatitis virus vectors to treat inherited enzyme deficiencies

**Immunological Memory** David Gray, Jonathan Sprent, 2013-03-07 Although

immunologists know rather a lot about the manifestation of immunological memory an understanding of the mechanism of memory at cellular and biochemical levels eludes us Indeed as we shall see it is not even clear which of the several models used to explain the working of memory approximates to the truth It is in order to report on approaches to this problem and on recent experimental advances in the field of memory cells that this volume has been put together In the past 4 5 years cell surface molecules that may enable us to define memory Band T cells have been identified It may now be possible to ask how memory cells are generated and to define what signals are required during or after antigenic encounter for a cell to enter the memory cell pool rather than to terminally differentiate into an effector cell The transition from virgin cell to memory cell is clearly accompanied by several biochemical changes For B cells isotype switching and somatic mutations leading to affinity maturation are well defined phenomena although the molecular mechanisms remain mysterious Both have received attention in many excellent reviews of late and so are not considered in detail in this book Neither switching nor somatic mutation is a feature of peripheral T cell maturation biochemical differences between virgin and memory T cells may only relate to differing activation requirements and possibly changes in the expression of accessory molecules

**Bluetongue Viruses** Polly Roy, Barry M. Gorman, 2012-12-06 Bluetongue viruses BTV cause diseases that have serious economic consequences in ruminants sheep cattle in many parts of the world The incidence of bluetongue disease affects the international movement of animals and germ plasm Although the etiological agent of the disease was isolated in 1900 and preliminary biochemical characterizations were published as early as in 1969 most of the current understanding of the molecular biology biochemistry and genetics of BTV has evolved only recently Triggered by the modern techniques of molecular biology genetics and immunology BTV research has experienced an information explosion in the past 10 years However much of this information is scattered throughout an extensive literature It is therefore an appropriate time to meld this together into a reference book This book includes comprehensive information on BTV research provided in articles contributed by researchers from around the world It covers what is known about the molecular structure of the virus and the current understanding of its biology evolution and relationships with its invertebrate and vertebrate hosts infection immunity and pathogenicity

**Neutralization of Animal Viruses** Nigel J. Dimmock, 2012-12-06 Understanding neutralization is particularly relevant to an appreciation of the interaction between a virus and its antibody synthesizing host since it is likely that viruses and the antibody system have evolved in response to reciprocally imposed selective pressures Neutralization of viruses which only infect non antibody synthesizing hosts while of considerable interest from of points of view is de facto without any such evolutionary significance a number of viruses of plants invertebrates vertebrates below fish in the evolutionary scale which do not synthesize antibody and most bacteria Viruses of organisms parasitic on or commensal with antibody synthesizing vertebrates such as enteric bacteria protozoa or metazoan parasites will be in contact with antibody at some stage of their existence and arthropod borne viruses which have a higher vertebrate as second host

are obviously bona fide members of the first category There is an urgent need to understand the principles by which antibodies inactivate virus infectivity since at present we are unable to rationally construct effective vaccines against new agents like the human immuno deficiency viruses or to improve existing vaccines The intention of this volume is to comprehensively review neutralization and where possible to construct a unifying theory which can be tested by experimentation

**Transmissible Spongiform Encephalopathies:** Bruce W. Chesebro, 2013-11-11 In spite of a long history of intense investigation the transmissible spongiform encephalopathies remain a poorly understood family of neurodegenerative diseases This group of diseases has been described in a wide variety of animal species and includes kuru Creutzfeldt Jakob disease and Gerstmann Straussler syndrome in humans and scrapie bovine spongiform encephalopathy and related syndromes in ruminants and rodents In all cases spongiform degeneration and astrogliosis are seen in specimens of brain and a filterable transmissible agent is present in the brain and some other tissues of affected individuals However the precise nature of this agent remains unknown Agent infectivity which can so far only be assayed by serial transmission to new individuals be remarkably resistant to inactivation has been shown to by heat chemicals and irradiation These properties create significant biohazard possibilities during exposure to infected tissues Transmission between humans was originally recognized in the unique epidemiology of kuru in New Guinea tribesmen and concern about transmission from animals to humans has re emerged as a result of the current epidemic of bovine spongiform encephalopathy in dairy cattle in Great Britain Although interspecies transmission has often been achieved experimentally its efficiency is highly variable There fore the possibility of spread of bovine spongiform encephalopathy from cattle to humans or various animal populations cannot be accurately predicted at this time This volume presents a comprehensive update of knowledge concerning the transmissible spongiform encephalopathies

**Borna Disease** Hilary Koprowski, W. Ian Lipkin, 2012-12-06 Borna disease was first described over 200 years ago in what is now Southeastern Germany as a fatal neurologic affliction of horses and was considered a curiosity for many decades The causative agent was unknown and the animal species infected in nature were limited to horses and sheep Today as described in this volume the host range has extended to all warm blooded animals the genes and proteins of the virus have been identified and many of the mechanisms responsible for behavioral disturbances are understood Serologic studies suggest that BDV or related agents are likely to play a role in human neuropsychiatric diseases

**Poxviruses** Richard W. Moyer, Peter C. Turner, 2012-12-06 The purpose of this volume is to highlight some current areas of poxvirus research which are likely to be particularly fruitful in the upcoming few years The first chapter by Drs Condit and Niles discusses poxvirus genetics Work in this area has provided mutants produced practical procedures to simplify the manipulation of viral genes and generated information about the molecular architecture and organization of genes characteristic of pox viruses One of the most intensively studied regions of the viral genome is the HindIII D region of vaccinia in which a combination of classical and molecular genetic analysis of the region has been particularly revealing



Within this region are open reading frames some of which are expressed early and others late organized in a fashion which is now known to be typical of these viruses Other studies related to temperature sensitive drug resistant and drug dependent mutants are also discussed Each of the other reviews included in this volume summarizes areas of research which have depended heavily on the genetics of the system The intracellular site of a poxvirus infection is mostly if not exclusively limited to the cytoplasm which dictates several interesting biological ramifications For example poxvirus transcription must occur in the cytoplasm rather than in the nucleus The virus copes with this situation by incorporating into the virion the enzymatic machinery necessary to initiate transcription from input virus

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