

TO THE CENTENNIAL OF A.A. BAYEV ONCOGENOMICS

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Serological Analysis of the Repertoire of Human Cancer Antigens and Autoantigens

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Abstract—The spectrum of human antigens allows a monitoring of various pathological processes such as autoimmune disorders and tumorigenesis. Serological analysis of cDNA expression libraries (SEREX) is now used to search for new cancer-associated antigens, which are potential diagnostic markers or targets for immunotherapy of cancer. The results obtained for several solid tumors are reviewed. Groups of antigens detectable by SEREX, causes of immunogenicity of autoantigens, and prospective implication of antigens in diagnostics and monitoring of cancer are discussed.

Key words: autoantigens, cancer immunodiagnostics, expression libraries, cDNA.

INTRODUCTION

Analysis of the repertoire of autoantigens may contribute to the understanding of mechanisms of various pathological processes, including autoimmune disorders and tumor transformation. Antigens changed in the course of tumor transformation may serve as diagnostic markers and targets of immune therapy.

To identify the antigens recognized by T cells, it is necessary to culture cytotoxic T cells of a patient [1]. The most convenient method to directly identify the antigens recognized by B cells is serological analysis of cDNA expression libraries (SEREX). This method has initially been proposed for a search for tumor antigens [2]. With SEREX, earlier unknown antigens have been identified in melanoma, breast cancer, colorectal cancer, Hodgkin's lymphoma, lung cancer, esophageal cancer, and several other tumors [2–5].

Here we summarize the results of our search for tumor antigens by SEREX.

EXPERIMENTAL PROCEDURES EMPLOYED IN OUR WORK

Sera were obtained from the Division of Combined Therapy, Blokhin Cancer Research Center and the Proctological Division, Moscow Hospital no. 24. To construct cDNA expression libraries, we used RNA

isolated from colorectal cancer cell lines LoVo and SW-480 and pooled testicular RNA of healthy subjects. With these preparations, cDNA was synthesized and cloned in the λ -ZAP expression vector as recommended by Stratagene (United States). Immuno-screening was carried out as described earlier [5, 6]. Allogenic screening was performed using serological mini-arrays of recombinant tumor antigens (SMART) [9]. Phage cDNA clones were converted to pBCKMV phagemid forms by *in vivo* excision as recommended by Stratagene. Plasmid DNA was purified and sequenced with fluorescent terminators by Sanger's method on an ABI Prism automated DNA sequencer (Perkin Elmer, United States).

SEREX ANALYSIS OF VARIOUS CANCER TYPES AND PATTERNS OF THE SEROLOGICAL RESPONSE

In SEREX, a cDNA library of a tumor is constructed with a phage expression vector. Recombinant proteins expressed on lytic infection are transferred onto a nitrocellulose membrane and incubated with autologous serum precleared of antibodies against bacterial and phage proteins. Clones displaying an immune response with a high IgG titer are selected and screened individually. Tumor specimens obtained by surgery are known to be contaminated with B cells and plasmacytes. As a result, such libraries contain

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Serologic Analysis of Human Cancer Antigens Steven A. Rosenberg, 1980 *Melanoma Antigens and Antibodies* Ralph A. Reisfeld, Soldano Ferrone, 2012-12-06 The ever expanding research on human cancer has resulted in numerous technical and conceptual advances during the last few years Serological structural and biological characterization of human melanoma constitutes one area of research that has received considerable attention from researchers and clinicians and has generated new and exciting information In this volume we have attempted to assemble work on topics that produced some of the most recent advances We asked each author to describe and interpret his most current research and whenever possible to compare and contrast it with work of other investigators in the field We have been careful not to impose our viewpoints except in contributions from our own laboratories since we want to provide the reader with as many divergent and sometimes opposing viewpoints as feasible Therefore we have not been overly concerned with overlaps in some individual topics We hope that this volume will provide the reader with a well balanced overview of current problems and ideas in a particular area of cancer research We wish to express our thanks to all contributors for their timely and very interesting manuscripts and we sincerely hope that the reader will enjoy this volume and benefit as much from it as we did R A Reisfeld S Ferrone La Jolla ix Contents CHAPTER 1 Immunogenetics of Melanoma RONALD T ACTON CHARLES M BALCH BRUCE BUDOWLE RODNEY C P Go JEFFREY M ROSEMAN SENG JAW SOONG AND BRUCE O BARGER 1 Introduction **Journal of the National Cancer Institute**, 1981 **JNCI, Journal of the National Cancer Institute** National Cancer Institute (U.S.), 1986 *Immunotherapy of Cancer* Mary L. Disis, 2007-10-28 Expert bench and clinical scientists join forces to concurrently review both the state of the art in tumor immunology and its clinical translation into promising practical treatments The authors explain in each chapter the scientific basis behind such therapeutic agents as monoclonal antibodies cytokines vaccines and T cells and illustrate their clinical manipulation to combat cancer Additional chapters address statistical analysis both of clinical trials and assay evaluations methods for the discovery of antigens adoptive T cell therapy and adaptive and innate immunity The challenges in clinical trial design the need for biomarkers of response such as novel imaging techniques and immunologic monitoring and the new advances and directions in cancer immunotherapy are also fully examined **Tumor Markers and Tumor-associated Antigens** Bimal C. Ghosh, Luna Ghosh, 1987 **Assessment of Tumour Response** Barry W. Hancock, 1982-12-31 The assessment of tumour response after treatment is one of the most important challenges in Oncology and the picture is so often complicated by the effects of therapy itself Clinical assessment is still by far the most important method of assessment at our disposal but there is increasing dependence on investigations of all types as indices of response This dependence may be misplaced if inappropriate investigations are pursued and we have tried to emphasise in this book the importance of selectivity Some indices of assessment e g tumour markers organ imaging have a vital role to play others e g histopathology genetics are assuming greater importance as tumour behaviour

becomes better understood One subject Immunology is still in its infancy as regards tumour follow up but shows much promise so that a full account of tumour immunology and trends in immunotherapy has been included I am grateful to Dr Brian Ross for his help with the chapter on Organ Imaging to the Department of Medical Illustration for their ever ready co operation with illustrations and photographs and to Miss Shirley Francis for doing much of the typing B W HANCOCK List of Contributors HANCOCK B W MD DCH MRCP Senior Lecturer in Medicine Honorary Consultant Physician Royal Hallamshire Weston Park Hospitals Sheffield U K NEAL F E KSG MBChB FRCR DMRT Consultant Radiotherapist Oncologist Weston Park Hospital Sheffield U K POTTER AM *Immunological Approaches to Cancer Therapeutics* Enrico Mihich, 1982 Clinical Management of Malignant Melanoma Giulio Costanzi, 2012-12-06 Where do you begin to look for a recent authoritative article on the diagnosis or management of a particular malignancy The few general oncology textbooks are generally out of date Single papers in specialized journals are informative but seldom comprehensive these are more often preliminary reports on a very limited number of patients Certain general journals frequently publish good in-depth reviews of cancer topics and published symposium lectures are often the best overviews available Unfortunately these reviews and supplements appear sporadically and the reader can never be sure when a topic of special interest will be covered Cancer Treatment and Research is a series of authoritative volumes which aim to meet this need It is an attempt to establish a critical mass of oncology literature covering virtually all oncology topics revised frequently to keep the coverage up to date easily available on a single library shelf or by a single personal subscription We have approached the problem in the following fashion First by dividing the oncology literature into specific subdivisions such as lung cancer genitourinary cancer pediatric oncology etc Second by asking eminent authorities in each of these areas to edit a volume on the specific topic on an annual or biannual basis Each topic and tumor type is covered in a volume appearing frequently and predictably discussing current diagnosis staging markers all forms of treatment modalities basic biology and more **Subject Index of Extramural Research Administered by the National Cancer Institute**, 1978 Current information about research grants and contracts supported by the National Cancer Institute Subject listing gives contract or grant number and topic Investigator grant number and contract number indexes Published Scientific Papers of the National Institutes of Health National Institutes of Health (U.S.), 1981 Each issue lists papers published during the preceding year Research Awards Index, 1979 *Subject Index of Current Extramural Research Administered by the National Cancer Institute*, 1978

Immunology of Malignant Diseases V.S. Byers, R. W. Baldwin, 2012-12-06 Over the past 5 years clinical immunology as a whole has advanced more rapidly than over the past 20 years Many of these advances have been due to monoclonal antibody technology with its ability to identify antigens on tumour cells with a precision never before available Monoclonal antibodies have the ability to identify subsets of human T lymphocytes and aid in diagnosis of both immunodeficiency disorders such as AIDS or autoimmune diseases and they can be adapted as drug targeting agents Additionally however

major advances have been made in identifying immunomodulating agents and the last year has seen two such agents IL 2 and OKT3 made available commercially for such intervention Furthermore another immuno modulating technique bone marrow transplantation ha now been established as a curative modality in leukaemia treatment A central issue in tumour immunology is whether human tumours express antigens which can be termed tumour specific This has important implications for both tumour immunity as well as drug targeting This issue is considered in detail by R A Robins in the introductory chapter in which the expression of antigens in human tumours is compared with that in experimentally induced animal tumours This controversial issue is also considered in later chapters by Bast in breast carcinoma Riimke and de Vries in melanoma V mky in lung cancer Armitage in colorectal cancer and Paulie and Perlmann in bladder carcinoma

Protides of the BIological Fluids H. Peeters,2014-11-26 *Protides of the Biological Fluids* Proceedings of the 30th Colloquium 1982 is a collection of manuscripts presented at the 30th Colloquium held in Brussels Belgium in 1982 This text is organized into three sections encompassing 160 chapters The first section highlights the mechanisms of the normal and abnormal mental function through evaluation of neuroproteins or the so called think proteins This section describes the manifestations clinical features diagnosis and therapeutic options of nervous system diseases The second section tackles monoclonal proteins as a reagent to detect antigens This section deals with the significant progress in cancer therapy and the binding of cytotoxic drugs to monoclonal antibodies The third section considers the potential of isodalt electrophoresis and high pressure liquid chromatography with particular emphasis on their application to protein analysis in biological fluids This book will be of great value to biochemists clinical chemists and clinicians

Cancer and Autoimmunity M.E. Gershwin,Yehuda Shoenfeld,2000-03-27 Of the two disciplines in parallel development for two decades tumor immunology and transplantation immunology the latter has thrived and has led to some of the most critical discoveries in immunobiology The former continues to thwart both scientists and clinicians alike The goal of immunologists in modern day research is to develop a simple and effective means to manipulate cancer in vivo possibly encompassing several venues identifying a phenotypic marker and the use of either active or passive immunization include the use of passive reagents carrying warheads to selectively destroy cancer cells or altering the basic process of cell survival This excellent multidiscipline authored volume presents a theme which has not been well described before The papers include both basic and clinical science and range from sophisticated molecular biology to little more than phenomenology e g the increased association of cancer in some autoimmune diseases and increased presentation of autoimmune phenomena in malignant condition This however is state of the art This collection of themes will be of use not only to bench scientists but also to clinicians who treat patients The book represents progress at the cutting edge of this discipline and points the way to further developments in the black box of immunology

National Cancer Institute Monograph National Cancer Institute (U.S.),1983

Adoptive Immunotherapy Burkhard Ludewig,Matthias W. Hoffmann,2008-02-02 An authoritative collection of optimal techniques for producing and

characterizing the immunologically active cells and effector molecules now gaining wide use in the clinical treatment of patients Taking advantage of the latest technologies the authors present readily reproducible experimental protocols for the study of dendritic cells T cells monoclonal antibodies and bone marrow transplantation The emphasis is on preclinical and clinical applications and on the progress of selected approaches in clinical trials Additional chapters cover the molecular definition of target antigens mathematical modeling approaches to immunotherapy and the utilization of regulatory T cells The protocols make it possible to study the adoptive transfer of tailored antigen specific immune cells and to improve the clinical application of adoptive immunotherapy

Therapeutic Opportunities and Innovative Biomarkers in Tumor Microenvironment Zhenyu Jia,Kexin Xu,Farah Rahmatpanah,2022-01-19 *Progress in Experimental Tumor Research*
Freddy Homburger,1967

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