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Serological Analysis of the Repertoire of Human Cancer Antigens and Autoantigens

E. P. Koroleva¹, M. A. Lagarkova², S. V. Khlgatian²,
Yu. V. Shebzukhov², A. A. Mescheryakov², M. R. Lichinitser²,
S. A. Nedospasov^{1,2}, and D. V. Kuprash¹

¹Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, 119991 Russia
E-mail: kuprash@online.ru

²Belozersky Institute of Physico-Chemical Biology, Moscow State University,
Moscow, 119899 Russia

³Blotkin Cancer Research Center, Russian Academy of Medical Sciences,
Moscow, 115478 Russia

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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 Journal of the National Cancer Institute, 1981 **JNCI, Journal of the National Cancer Institute** National Cancer Institute (U.S.), 1986 *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

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 **Immunological Approaches to Cancer Therapeutics** Enrico Mihich, 1982 *Immunoproteomics* Kelly M. Fulton, **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

Biological Response Modifiers, 1983 *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

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