



# **MONOCLONAL ANTIBODIES IN CANCER**

Edited by

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## Preface

This represents the third volume in a series on cancer markers published by the Humana Press. The first volume, published in 1980, stressed the relationship of development and cancer as reflected in the production of markers by cancer that are also produced by normal cells during fetal development. The concept that cancer represents a problem of differentiation was introduced by Barry Pierce in describing differentiation of teratocarcinomas. Highlighted were lymphocyte markers, alphafetoprotein, carcinoembryonic antigen, ectopic hormones, enzymes and isozymes, pregnancy proteins, and fibronectin.

The second volume, published in 1982 and coedited with Britta Wahren, focused on the diagnostic use of oncological markers in human cancers, which were systematically treated on an organ by organ basis. At that time, the application of monoclonal antibodies to the identification of cancer markers was still in a very preliminary stage. A general introduction to monoclonal antibodies to human tumor antigens was given there by William Raschke, and other authors included coverage of those markers then detectable by monoclonal antibodies in their chapters.

Since the appearance of the second volume there has been an exponential increase in the number of papers published in which monoclonal antibodies have been used to identify cancer markers. This justifies, in part, the award of the 1984 Nobel Prize in which Köhler and Milstein shared. In less than 10 years, the technique of cell hybridization described by Kohler and Milstein [*Nature* **256**, 495 (1975)] has been modified, adapted, transformed, and applied not only to the identification of cancer markers, but also to the identification of microbial and normal tissue molecules, as well as to the provision of highly specific tools for the unraveling of many biological and pathological processes. In view of the decisive impact made by monoclonal antibodies on biological research, it came as no surprise that Köhler and Milstein shared the 1984 Nobel Prize in medicine.

In this third volume, the editors have attempted to update the vast amount of new information that is rapidly accumulating because of the widespread application of monoclonal antibodies in the study, diagnosis,

treatment, and prevention of cancer. The book begins with a brief review of the use of monoclonal antibodies in animals, and continues with the human system on which monoclonal antibodies have possibly made their greatest impact to date, that is, melanoma antigen. In this chapter the molecular characterization of melanoma markers made possible by monoclonal antibodies is presented by coeditor, Ralph Reisfeld, and the theme recurs with variations in subsequent chapters. In addition, the application of monoclonal antibodies to diagnosis is emphasized and the present status of the use of monoclonal antibodies in cancer therapy, now carried out in many laboratories, is presented.

A short history of cancer markers is given in the accompanying table. We feel that the main impact of monoclonal antibodies on cancer and cancer markers is still emerging, and many cancer markers of the future remain still to be discovered. In addition, monoclonal antibodies may also be used to understand the basic biology of cancer and carcinogenesis. As an example, our definition of cancer markers must now also include chromosomal changes that are currently being identified at new levels by ever more sophisticated methods. In the future, by probing for "oncogenes" or oncogene products, even more precise cancer markers should be found. In fact, monoclonal antibodies may prove to be an effective tool to identify oncogene products not yet identifiable.

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A Short History of Cancer Markers

Year	Author	Markers
1846	H. Bence-Jones	Bence-Jones protein
1928	W. H. Brown	Ectopic hormone syndrome
1930	B. Zondek	HCG
1932	H. Cushing	ACTH
1933	Gutmann and Gutmann	Prostatic acid phosphatase
1949	K. Oh-Uti	Deletion of blood group antigens
1959	C. Markert	Isozymes
1960	P. Newell	Philadelphia chromosome
1963	G. I. Abelev	Alphafetoprotein
1965	Gold and Freeman	Carcinoembryonic antigen
1969	Heubner and Todaro	Oncogenes
1975	Kohler and Milstein	Monoclonal antibodies
1980	Cooper, Weinberg, Bishop, etc.	Oncogene probes and transfection
1981	J. Yunis	Fragile sites

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# Chapter 1

## Monoclonal Antibody Defined Antigens on Animal Tumors

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### 1. Introduction

Monoclonal antibodies to both experimental animal tumors and human tumors have been developed concurrently. Clearly most attention has focused upon human tumors, since antibodies specifically, or more commonly preferentially, reactive with these have diagnostic and therapeutic applications. However, because the basic immunology of experimental animal tumors, including the expression and occurrence of tumor-associated antigens, is considerably more defined, it is pertinent to assess the performance of monoclonal antibodies to these tumors.

Monoclonal antibodies represent powerful probes to dissect numerous problems in tumor immunology and the cellular and molecular biology of cancer, previously unapproachable using conventional methodology. However, since they are only tools for the researcher, they do not elaborate the concepts, but can only be employed for their resolution. The aim of this review therefore is to examine the application of monoclonal antibody technology in the study of antigens associated with experimental tumors and to identify those areas of research in which these reagents have proven or potential usage.