ADVANCES IN COMPARATIVE LEUKEMIA RESEARCH 1979

DAVID S. YOHN, BORIS A. LAPIN, and
JAMES R. BLAKESLEE
Editors

ADVANCES IN COMPARATIVE LEUKEMIA RESEARCH 1979

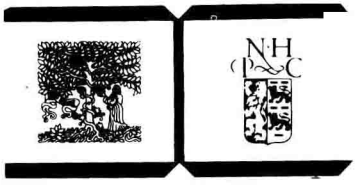
Proceedings of the IXth International Symposium on Comparative Research on Leukemia and Related Diseases, held in Pitsunda, U.S.S.R. on 3-6 October, 1979

Editors:

DAVID S. YOHN (Secretary General, IACRLRD)
Director, The Ohio State University Comprehensive Cancer Center, Columbus, Ohio, U.S.A.

BORIS A. LAPIN (President, IACRLRD)
Director, Institute of Experimental Pathology and Therapy, Sukhumi, U.S.S.R.

JAMES R. BLAKESLEE (Editorial Associate, IACRLRD)
Associate Professor, The Ohio State University Comprehensive Cancer Center, Columbus, Ohio, U.S.A.



ELSEVIER/NORTH-HOLLAND
NEW YORK • AMSTERDAM • OXFORD

Published by:

Elsevier North Holland, Inc.
52 Vanderbilt Avenue, New York, New York 10017

Sole distributors outside U.S.A. and Canada:

Elsevier/North-Holland Biomedical Press
335 Jan van Galenstraat, P.O. Box 211
Amsterdam, The Netherlands

Library of Congress Cataloging in Publication Data

International Symposium on Comparative Research on Leukemia and Related Diseases, 9th, Pitsunda, Georgia, 1979.
Advances in comparative leukemia research, 1979.

Bibliography: p.
Includes index.
1. Leukemia—Congresses. 2. Pathology, Comparative—Congresses. I. Yohn, David S. II. Lapin, Boris Arkad'evich. III. Blakeslee, James R. IV. Title. [DNLM: I. Leukemia—Congresses. W3 IN916XE 9th 1979a / QZ350 I6153 1979s]
RC643.I523 1979 616.9'9419 79-27554
ISBN 0-444-00378-9

Manufactured in the United States of America

INTERNATIONAL ASSOCIATION FOR COMPARATIVE RESEARCH ON LEUKEMIA AND RELATED DISEASES

WORLD COMMITTEE

Past Presidents of the World Committee

Gustaf Rosenberger, West Germany	1963 - 1969
Ray M. Dutcher, U.S.A.	1969 - 1971
Luigi Chieco-Bianchi, Italy	1971 - 1973
Yohei Ito, Japan	1973 - 1975
Johannes Clemmesen, Denmark	1975 - 1977
Peter Bentvelzen, The Netherlands	1977 - 1979

Officers of the World Committee 1979 - 1981

Boris Lapin, President
Institute of Experimental Pathology and Therapy
Gora Trapetziya, Sukhumi
Georgia, U.S.S.R.

Peter M. Biggs, Vice President
Houghton Poultry Research Station
Houghton, Huntingdon PE17 2DA
Great Britain

David S. Yohn, Secretary General
Ohio State University Cancer Center
1580 Cannon Drive, Suite 357
Columbus, Ohio 43210 U.S.A.

Walter S. Graulich, Treasurer
The Bank of New Jersey
P.O. Box 430
Moorestown, New Jersey 08057 U.S.A.

Roger R. Stinehart, General Counsel
Gingher & Christensen
311 East Broad Street
Columbus, Ohio 43215 U.S.A.

Members of the World Committee 1979 - 1981

Heinz Bauer
Institut fur Virologie
Fachbereich Humanmedizin
Frankfurter Strasse 107
6300 Giessen, West Germany

Peter Bentvelzen
Radiobiological Institute TNO
151 Lange Kleiweg, Rijswijk (ZH)
The Netherlands

Luigi Chieco-Bianchi
Istituto di Anatomia e Istologia Patologica
Universita Degli Studi
Via A. Gabelli, 61
35100 Padova, Italy

Guy de Thé
Programme CNRS
Faculté de Médecine Alexis Carrel
Rue Paradin
69372 Lyon Cedex 2, France

Friedrich Deinhardt
Max V. Pettenkofer-Institut
Pettenkoferstr. 9a
8000 Munchen 2, West Germany

Jes Forchhammer
The Fibiger Laboratory
Ndr. Frihavnsgade 70
DK 2100 Copenhagen O, Denmark

IXth INTERNATIONAL SYMPOSIUM PROGRAM COMMITTEE AND INVITED ORGANIZERS

Honorary Symposium Chairman — John Moloney, NCI, U.S.A.
Program Chairman — Boris Lapin, NAMS, U.S.S.R.

IACRLRD Program Committee

Peter Bentvelzen, The Netherlands
Peter Biggs, Great Britain
Friedrich Deinhardt, West Germany
Guy de Thé, France
Rose Ruth Ellison, U.S.A.
Boris Lapin, U.S.S.R.
John Moloney, U.S.A.
Máire Mulcahy, Ireland
David Yohn, U.S.A.

Symposium Session Chairmen

Frank Ruscetti, U.S.A.
Yoji Ikawa, Japan
Jan Svoboda, Czechoslovakia
Marvin Rich, U.S.A.
Rudolf Ippen, East Germany
Harry Abelev, U.S.S.R.
Bruce Calnek, U.S.A.
Lelita Yakovleva, U.S.S.R.
Margarette Khokhlova, U.S.S.R.
V.P. Shishkov, U.S.S.R.
August Garin, U.S.SR.
Noriaki Ida, Japan
Max Essex, U.S.A.

Symposium Session Moderators

Alexander Fridenstein, U.S.S.R.
Viktor M. Zhdanov, U.S.S.R.
Günter Pasternak, East Germany
Nikolay Mazurenko, U.S.S.R.
Richard Heberling, U.S.A.
Rose Ruth Ellison, U.S.A.
Máire Mulcahy, Ireland

Symposium Session Rapporteurs

Ger van den Engh, The Netherlands
Peter Bentvelzen, The Netherlands
Ray Gilden, U.S.A.
Harvey Rabin, U.S.A.
Judith Bader, U.S.A.
Anton Hagenbeek, The Netherlands
Clyde Dawe, U.S.A.

IXth INTERNATIONAL SYMPOSIUM FOR COMPARATIVE RESEARCH ON LEUKEMIA AND RELATED DISEASES

Organizing Committee, U.S.A.

D. S. Yohn, Secretary General
OSU Comprehensive Cancer Center

W. S. Graulich, Treasurer
The Bank of New Jersey

J. R. Blakeslee, Assistant
OSU Comprehensive Cancer Center

R. R. Stinehart, General Counsel
Gingher & Christensen

H. Willsey, Liaison
Leukemia Society of America, Inc.

L. R. Sibal, Liaison
National Cancer Institute

K. White, Publicity
Leukemia Society of America, Inc.

P. Newman, Publicity
National Cancer Institute

C. Love, Assistant
IACRLRD

S. Hixson, Assistant
IACRLRD

M. Stinehart, Assistant
IACRLRD

K. Fletcher, Assistant
IACRLRD

D. White, Transportation
Columbus Automobile Association

J. McHugh, Transportation
Columbus Automobile Association

Organizing Committee, U.S.S.R.

B. A. Lapin, Chairman

E. K. Dzhikidze, Co-chairman

N. A. Fedorov

R. A. Kukajn

V. P. Shishkov

N. P. Mazurenko

F. I. Ershov

Ts. S. Makalatiji

A. K. Kiseljov

V. I. Platonenko

S. S. Debov, Co-chairman

M. P. Khokhlova, Co-chairman

N. A. Kraevski

O. K. Gavrilov

F. L. Kiseljev

I. N. Krukova

V. D. Kiknadze

L. A. Yakovleva

M. I. Saveljev

A. I. Shepelev

B. I. Milan

Dedication of the Proceedings of the IXth International Symposium for Comparative Research on Leukemia and Related Diseases

These proceedings are dedicated to the sponsoring organizations and to the participants who contributed to the unique success of the first open exchange in history between almost equal numbers of leukemia research scientists from socialist and capitalist countries. Approximately 300 clinical and basic scientists spent nearly five days cloistered on the shore of the Black Sea in Pitsunda, Russia to exchange formally and informally their latest findings in laboratory, clinical, and epidemiologic research. These participants by country are listed in the preliminaries of this volume.

The major sponsoring agencies and institutions who were convinced of the compelling need for this scientific exchange in Russia at this time in medical and scientific history were:

- The National Cancer Institute - USA
- The Leukemia Society of America, Inc. - USA
- The National Academy of Sciences - USSR
- The Institute of Experimental Pathology and Therapy - USSR
- The Cancer Research Institute, Moscow - USSR

Joining these major sponsors were all the institutions worldwide who contributed by supplying in part the individual expenses incurred by the participating scientists from their institution. And contributing indirectly by offsetting operating expenses of the Secretariat (USA) were:

- Burroughs-Wellcome Company
- Litton Bionetics, Inc.

The planning of this meeting in the USSR began nearly eight years ago by two members of the World Committee, Frank J. (Dick) Rauscher, then director of the National Cancer Institute, USA, and now just retiring from the World Committee, and Boris Lapin, Director of the Institute of Experimental Pathology and Therapy, USSR, and newly elected President of IACRLRD. In addition, significant were the more recent efforts of John Moloney and Louis Sibal of the National Cancer Institute, USA and of Arthur Upton, Director of NCI. The support of the Leukemia Society of America (LSA) was represented by among others, Rose Ruth Ellison, and Kenneth McCredie past and current Vice President, respectively, of the Medical and Scientific Advisory Committee of LSA. Both presented important status reports on leukemia therapy in the USA at the meeting.

And key to the availability of financial support from the USSR was the efforts, in addition to those of Boris Lapin, of Nikolai Blokhin, President of the National Academy of Medicine - USSR and Director of the Cancer Research Institute, Moscow.

The contribution of these individuals and their respective organizations made possible the fulfilled desire of dedicated scientists to share their findings with one another regardless of political systems. In the last analysis the success of the meeting is attributed to their enthusiastic participation.

David S. Yohn, Ph.D., M.P.H.
Editor and Secretary General, IACRLRD
Director, Ohio State University
Comprehensive Cancer Center

IXth INTERNATIONAL SYMPOSIUM PARTICIPANTS

ARGENTINA

Christiane Pasqualini

BELGIUM

Arsenè Burny
Paul Jacquemin
Marc Mammerickx

BRAZIL

Carlos Romero

BULGARIA

Z. Mladenov
B. Serafimov-Dimitrov
I. Todorov

CANADA

Jean Joncas
José Menezes
R.A. Sonstegard
Mark Wainberg

CZECHOSLOVAKIA

J. Bubeník
I. Hložánek
K. Smetana
J. Svoboda
J. Hirsch
Ch. Altaner
M. Travnicek
J. Závada
Z. Závadová
P. Rauko

DENMARK

Peter Ebbesen
Jes Forchhammer

FEDERAL REPUBLIC OF GERMANY

Heinz Bauer
Rolf Flügel
Elisabeth Gateff
Rüdiger Hehlmann
Gerhard Krueger
R. Neth
Ulrich Neumann
S. Thierfelder
Hans Wolf
V. Erfle
Hans Rodt

FRANCE

Georges Balouet
Chantal Godard
F. Coudert

GERMAN DEMOCRATIC REPUBLIC

R. Ippen
D. Höche
J. Hermann
F. Zintl
H. Konrad
H. Libermann
M. Rudolph
H. Stobbe
K. Wutke
J. Millek
V. Wunderlich
P. Venker
R. Subert

GREAT BRITAIN

Peter Biggs
M.A. Epstein
Melvyn Greaves
P.C. Powell

HUNGARY

I. Farkach
F. Tóth
L. Váczi

IRELAND

Máire Mulcahy

ISRAEL

Ze'ev Trainin

ITALY

Luigi Chieco-Bianchi
Aurora Costa
Anita de Rossi
Angelo Nicolin
Rosella Silvestrini

JAPAN

Noriaki Ida
Yoji Ikawa
Yohei Ito
Koshi Maruyama
Misao Onuma
Toyoro Osato

POLAND

P. Kúsnierczyk
Cz. Radzikowski

THE NETHERLANDS

Peter Bentvelzen
G. de Boer
A. Hagenbeek
Cees Melief
Benita Plesch
Ger van den Engh
Leo Van Griensven
A.J.P. Veerman

SWEDEN

Eva-Marie Fenyo
Olle Ljungberg

USA

Dharam Ablashi
Hans Adldinger
Jose Azocar
Judith Bader
Roberta Black
James Blakeslee
John Blasecki
Ernest Borek
Bruce Calnek
William Campbell
James Chan
Kenneth Chang
Young Chen
Tom Chin
Jack Chirikjian
Lyman Crittenden
Muthiah Daniel
Clyde Dawe
Louis Delanney
Sushilkuma Devare
William Dodge
James T. Duff
James L. East
Rose Ruth Ellison
Ray Erikson
Myron Essex
Aly M. Fadly
Emil Freireich
Richard Gatti
Murray Gardner
Raymond Gilden
Tin Han
William Hardy
John Harshbarger

USA, Continued

Jean Carol Hager
James Hazdra
Richard Heberling
Edward Hoover
Rashida Karmali
Thomas Kawakami
Sylvia Kerr
Paul Kimball
William Kundin
Kenneth Lam
E.W. Lamon
Christine Li
Thomas Mack
John MacMillan
Kenneth McCredie
Hans Meier
Richard Metzgar
Harry Milman
Nirmal Mishra
John Moloney
Malcolm Moore
Herbert Morgan
Faramarz Naeim
James Nance
Russell Neubauer
Richard Olsen
Bijay Pal
Takis Papas
Gary Pearson
John Portis
Wolf Prensky
Louis Qualtiere
Harvey Rabin
Celestina Raineri
Suraiya Rasheed
E.P. Reddy
Frederick Reynolds
J.S. Rhim
Marvin Rich
Jennifer Rojko
Pradip Roy-Burman
Ivor Royston
Francis Ruscetti
Sandra Ruscetti
M.G. Sarngadharan
K.A. Schat
Martin Sevoian
Louis Sibal
B.I.S. Srivastava
Richard Steeves
Robert Ting
James Whitman
David Yohn

USSR

A.I. Ageenko
F.I. Adzhigitov
A.D. Altshtein
E.A. Andrijan
B.M. Bergolts
B.D. Bronds
Z.A. Butenko
T.I. Bulichova
S.N. Bykovskaya
I.M. Chumakov
G.I. Deitchman
N.A. Fedorov
A.Y. Friedenstein
F.E. Fainstein
N.P. Goncharov
O.K. Gavrilov
L.V. Indziya
K.V. Iljin
L.G. Kovaleva
I.V. Koshel
R.N. Korovin
M.P. Khokhlova
D.V. Karlikov
G.F. Koromyslov
P.N. Kosyakov
I.N. Kogarko
R.A. Kukain
E.I. Khomchenovsky
U.I. Kudryavets
I.N. Krukova
B.A. Lapin
V.N. Lebedev
D.S. Markaryan
N.P. Mazurenko
L.A. Machonova
A.E. Nadareishvily
V.G. Nesterenko
T.A. Posevaya
M.I. Parfanovich
I.V. Rakovskaya
D.Y. Solovey
A.V. Sergeev
V.N. Stepina
A.I. Shikov
M. Sh. Sheklashvily
A.L. Shengelaya
V.P. Shishkov
V.Y. Shevlagin
Z.V. Shevtsova
Z.F. Terebkova
V.S. Ter-Grigorov
L.A. Tarasishin
A.G. Tatosyan
E.B. Vladimirskaya
A.F. Voevodin
L.A. Yakovleva

PREFACE

The unique feature of the Proceedings of the IXth International Symposium for Comparative Research on Leukemia and Related Diseases, is that it contains reports from nearly a hundred basic and clinical sicentists from Socialist countries together with an even larger number of reports from similar scientists from Western Europe, the Americas, and Asia.

This symposium in keeping with previous symposia, continues the tradition of emphasizing comparative aspects of leukemia research. Recorded in these proceedings and its predecessors is the repository of our progress in understanding and controlling leukemia and related diseases.

The nearly two decades in which these symposia have been held have witnessed the emergence of cures in human leukemia, primarily through the use of combination chemotherapy, supportive maintenance therapy, and judicious use of radiotherapy when required. Testimony to this happy development occurs in reports of the sessions devoted to clinical, immunologic, and epidemiologic studies.

Complementing the progress made in therapy of human leukemia are the revealing studies on the biology and molecular genetics of leukemia cells and the role of viruses and viral genes in the etiology of animal leukemias as reported by the participants.

Of particular significance in this volume is the status of studies of leukemia and related diseases in poikilotherms ranging from mollusks to amphibians, as highlighted by the review by Clyde Dawe.

This volume contains capsulized reports of all presentations whether given orally or as posters. A companion volume to be published in Russia contains full length papers of all contributions from the Socialist countries.

David S. Yohn, Ph.D., M.P.H.
Secretary General

OPENING ADDRESS

JOHN B. MOLONEY,* Ph.D.
Honorary Chairman of the IX International Symposium on Comparative Research on Leukemia and Related Diseases

"SOME ADVANCES IN RESEARCH ON LEUKEMIA AND RELATED DISEASES"

Mr. Chairman, members of the Organizing Committee, permit me to express my gratitude for being recognized as the Honorary Chairman of this the IXth International Symposium for Comparative Research on Leukemia and Related Diseases.

The IXth Symposium! It was in 1963 when the first meeting of the World Committee for Comparative Leukemia Research was held in Hanover, Germany. Since its inception, the Committee, through the International Association, has fostered the development, the coordination, the dissemination of research data derived from the study of leukemia and related diseases in animals and man. In part, this has been accomplished by sponsoring these International Symposia, held every two years, and in part through the publication of the proceedings of the Symposia.

What then has been accomplished over the last 16 years? To what extent have advancements been made in our understanding of the etiology of cancer, in the diagnosis and the treatment of human neoplasia?

TREATMENT RESEARCH

This, of course, includes all aspects of treatment involving individual cancer patients or groups of patients (I will note but a few advances in a few cancers.).

Acute Leukemia: This is the major cause of cancer death in children under the age of fifteen. In the past fewer than five percent of all children diagnosed with the disease survived five years. Today, with total therapy utilizing combinations of drugs and prophylactic radiation to the brain, more than 90% of children with acute leukemia achieve a complete response, and 50% of them are alive at 5 years.

Breast Cancer: This is the major cause of cancer deaths for women in the United States. Each year approximately 105,000 women are diagnosed as having the disease; 13,000 are under 45 years of age. Two studies have shown the benefit of instituting drug therapy early in the course of

*Dr. Moloney is an Assistant Director, National Cancer Institute, USA

treatment - i.e., soon after mastectomy. In one study 65% of a group of patients who received the drug L-PAM after surgery are free of disease at 4 years, whereas only 43% of the control group are free of disease at the same time interval. A similar study carried out in Milan, Italy, showed that 73% of a group of breast cancer patients who received a 3-drug combination after surgery are free of disease at 3 years. In contrast, 48% of the controls are alive and disease free at 3 years. Similar results are achievable in post-menopausal patients. These clinical trials in breast cancer are important because they have demonstrated that the use of post operative chemotherapy is feasible and that it works.

Before combination or multi-modality therapy was developed, virtually no patient with advanced Hodgkins' Disease survived beyond 5 years. Today, through the use of radiotherapy and/or combination drug treatment, the oncologist is able to produce complete remissions in 80% of adult patients with advanced Hodgkins' Disease. Again, similar results have been shown in patients with diffuse Histiocytic Lymphoma.

The continued rapid exchange of information via collaboration between the laboratory and the clinic, will yield new and different methods for treating all cancers, particularly those which are almost totally resistant to all current treatments. One of the most exciting research areas for the future is the use of biological materials in the treatment of cancer, such as the lymphokines, interferon and thymosin. It appears, in fact, that these do play a role in the regulation of the growth of cancer.

DETECTION AND DIAGNOSIS

Over the last 16 years, highly significant advances have been made in all aspects of Cancer Detection and Diagnosis. The use of X-ray mammography has proved its value in the early detection of breast cancer. The development of Computer Assisted Tomography (CAT) is a major advance in cancer diagnosis, as well as the use of ultrasound, which holds great promise as an effective noninvasive diagnostic tool. Regarding cytologic aspects of detection - the most widely used screening test for cancer is the Papanicolaou smear for detection of cancer of the uterine cervix. Now there is renewed interest in the use of sputum cytology to detect early lung cancer in high risk groups, such as middle aged male cigarette smokers. To facilitate these studies, cell-sorting machines have been developed with ability to separate normal and cancer cells. Similarly, an advanced computer controlled high resolution scanning microscope has been developed which

has the capability of recalling previously chosen cells for reexamination and analysis.

What of the epidemiologic approaches to diagnosis and early detection? These have been used to identify high risk groups in prospective studies to prove the value of various methods of intervention, as in a large ongoing early lung cancer detection study. However, in this study one of the unforseen events is that some bronchial cancers are multicentric, thus removal of one lesion is really of no help to the patient. Indeed, in this situation early detection will increase the time to ultimate outcome but will have no effect on the time from inception of the tumor to outcome.

CANCER ETIOLOGY

How far have we come in defining the etiology, the cause or causes of cancer in animals and man? Let us first consider chemical and physical carcinogenesis. Sixteen years ago we had very little knowledge of the metabolism of certain chemical compounds and of the intrinsic mechanisms of carcinogenesis. Only limited research was conducted on chemical and physical agents and substances thought to be or known to be active in cancer causation. All aspects of environmental, occupational and industrial carcinogenesis were considered - shall we say - superficially.

In recent years chemical carcinogenesis has received increased attention, as it has become clear that environmental chemicals play, at a minimum, a contributory role in the etiology of many cancers. As research in this area has become increasingly sophisticated, more effective model systems have been developed to detect and assay carcinogens, to study their metabolism in vivo and in vitro, to analyze the mechanisms by which they initiate and promote cancer, and to find ways in which their action can be blocked or reversed. In this respect, the metabolic pathways of carcinogen activation and deactivation have been found to be qualitatively similar in humans and in experimental animals. However, there is a wide quantitative variation among individuals.

The development of effective, rapid assays has been important in the progress of all stages of research in chemical carcinogenesis. The Ames mutagenesis system has been of extreme value in qualitative studies on concurrent exposure to several carcinogens which show marked synergistic or inhibitory activity. These studies are of practical significance in that many population groups are repeatedly exposed to combinations of carcinogens. Recently, an extremely sensitive radioimmunoassay was developed which

will measure femtogram (10^{-15}gms) quantities of various antigens. This is being used in molecular studies of viral-chemical cocarcinogenesis and to study variation in DNA-carcinogen binding patterns.

Today, the two stage mechanism of carcinogenesis is well established for skin and there is evidence for its existence in other organs. The first stage, initiation, effects a permanent, heritable change in the cell. The second stage, promotion, completes the malignant transformation. This mechanism may explain the long latent period between exposure and appearance of tumor as in human prenatal exposure to X-ray or certain chemicals like diethylstilbesterol (DES), which can result in malignancy many years after birth.

A new and exciting area of research in chemical carcinogenesis is Chemoprevention, specifically the use of retinoids, synthetic analogues of Vitamin A to prevent the development of invasive cancer. Retinoids have been shown to be highly potent in prevention of malignant transformation of cells in vitro whether the carcinogenic agent be polycylic hydrocarbons, radiation, or growth factors induced by oncogenic viruses. Additionally, new synthetic retinoids which are markedly less toxic and more potent than 13-cis-retinoic acid, can prevent breast cancer and bladder cancer in experimental animals. These findings suggest that further clinical trials be considered.

Let us now consider Biological Carcinogenesis or Viral Oncology. In 1963, the only oncogenic viruses available for study were the polyoma virus, the rabbit Papilloma virus, MMTV, a few Murine leukemia viruses and, of course, the Avian tumor viruses. The Murine sarcoma viruses had not been isolated, and EBV was very much a question mark. Indeed, much effort was being directed toward the development of a virus-induced tumor system in primates.

Over the last one and a half decades there has literally been an explosion of knowledge from the field of Viral Oncology. Today there are available for investigation virus-tumor systems which include amphibians, birds, the murine, feline, bovine and sub-human primates.

In the course of study on the human primate system, it has become apparent that viruses as nice little round entities are not necessarily involved in malignancy - rather through the application of sophisticated molecular and immunological techniques, it is increasingly likely that viral information as specific nucleic acid sequences in the genome of human cells is intimately involved with neoplasia. These sequences

triggered by chemical exposure. radiation or still another virus infection, can direct the synthesis of a protein or proteins responsible for malignant transformation. Where appropriate systems have been developed, the carcinogenic activity of chemical and physical agents is found to be associated with the activation of viral genes.

Several developments have occurred which emphasize the central role that viral information plays in human cancer and underscores the enormous value of research in viral oncology in understanding the basic mechanisms of carcinogenesis:

The isolation of specific proteins responsible for transformation and the identification of the viral genetic sequences that code for them provide defined reproducible systems for the study of oncogenic mechanisms. Further studies on the recombination of genetic sequences permits in depth examination of those factors regulating the expression or genesis of biological carcinogens.

A phosphorlyated protein P-21 has recently been isolated from the sarcoma virus systems of Kirsten and Harvey. This protein coded for by the SRC gene is the first mammalian viral gene product which has been proven to be responsible for the maintenance of the transformed state. Another interesting and related finding is the characterization of Kirsten sarcoma virus related rat sequences, which are expressed at high levels in chemical-carcinogen induced rat mammary tumors; these sequences include that portion of the viral genome that codes for P-21. This has obvious implications in the development of rapid assays for chemical carcinogens.

A class of revertant cells has been isolated which contains active feline sarcoma virus, yet has the phenotypic properties of normal cells in vivo and in vitro. Thus, this system in which transformation is blocked by cellular regulation of the viral genome, provides and excellent model for the study of the control of malignant potential.

Utilizing two different methods of detection, evidence is accumulating that human breast tumors contain an antigen which cross reacts with GP-52, of the mouse mammary tumor virus. These findings are highly significant in that they may provide diagnostic and prognostic tests for human mammary cancer.

The DNA viruses continue to be of major importance in cancer research. Serological, epidemiological and molecular hybridization studies have firmly established the association of EBV with nasopharyngeal carcinoma and with Burkitts lymphoma. The appearance of specific EB viral markers