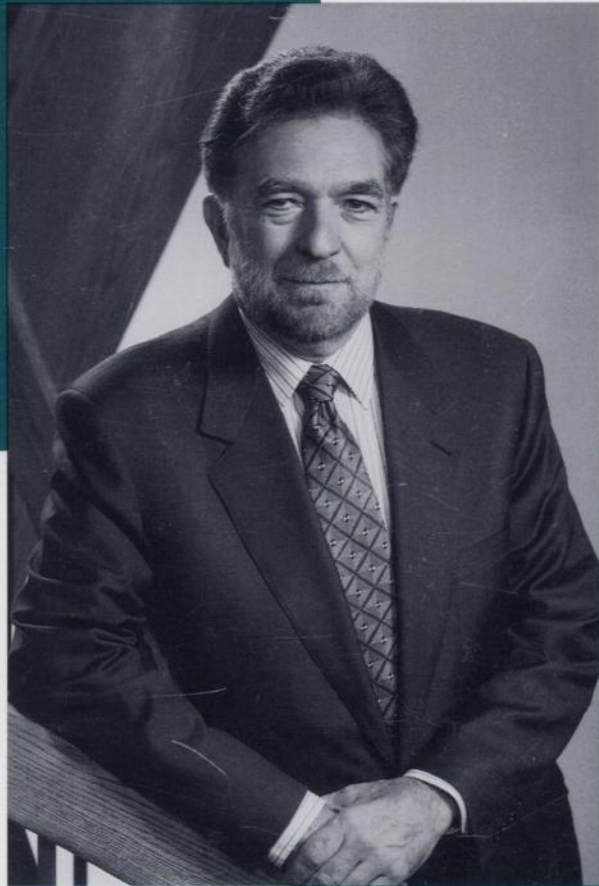




Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH



May 15, 1995
Volume 55 • Number 10
PP. 2007-2223
ISSN 0008-5472 • CNREA 8

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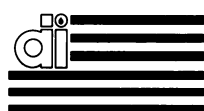
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*To determine the safety and efficacy of "antisense"
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ENTRY CRITERIA INCLUDE:

- *Chronic Myelogenous Leukemia-Chronic Phase*
- *Chronic Myelogenous Leukemia-Blast Crisis*
- *Refractory Acute Myeloid Leukemia*

For information regarding eligibility contact:

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"In Vivo and in Vitro Analysis of..."

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Hardware, Operating system, Software

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CANCER AND THE CELL CYCLE



Joint Conference of the
American Association for Cancer Research
and the
Swiss Institute for Experimental Cancer Research



January 17-20, 1996
Centre Hospitalier Universitaire Vaudois (CHUV)
Lausanne, Switzerland

CONFERENCE CHAIRPERSONS

Edward E. Harlow / Charlestown, MA
Viesturs Simanis / Lausanne, Switzerland

SCIENTIFIC PROGRAM

Introduction

Tim Hunt / Herts, England
Paul Nurse / London, England

Coordination of S Phase and M Phase

Kim Nasmyth / Vienna, Austria
John Diffley / Herts, England

Control of CDKS (Part 1)

David Beach / Cold Spring Harbor, NY
Charles J. Sherr / Memphis, TN
Stephen J. Elledge / Houston, TX

Control of CDKS (Part 2)

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C. Lehner / Tübingen, Germany
Matthias Peter / San Francisco, CA
Erich A. Nigg / Epalinges, Switzerland

Checkpoints

Andrew Murray / San Francisco, CA
Anthony Carr / Brighton, England
Viesturs Simanis / Epalinges, Switzerland

G1 Progression in Higher Eukaryotes

Edward E. Harlow / Charlestown, MA
David M. Livingston / Boston, MA
Robert A. Weinberg / Cambridge, MA
Rene Bernards / Amsterdam, The Netherlands
Charles Sherr / Memphis, TN
C. Lehner / Tübingen, Germany

The Role of *myc* in Life and Death

Robert Eisenmann / Seattle, WA
Gerard I. Evan / London, England
Bruno Amati / Epalinges, Switzerland

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Arnold J. Levine / Princeton, NJ
Michael B. Kastan / Baltimore, MD
David P. Lane / Dundee, Scotland
Richard Iggo / Epalinges, Switzerland

Meeting Summary

Benjamin Lewin / Cambridge, MA

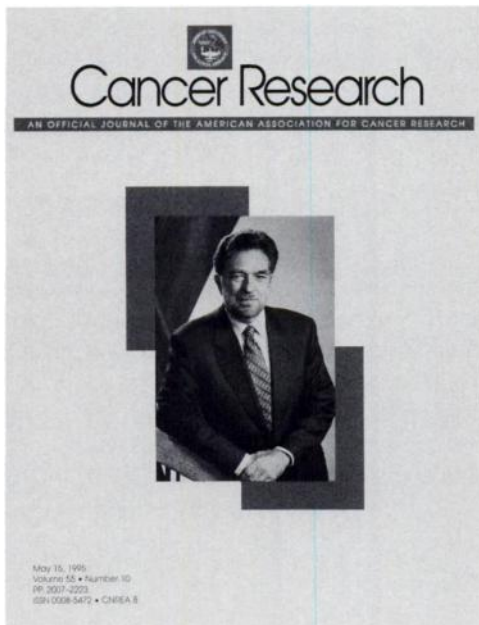
Additional Speakers to be Announced

*Applicants are encouraged to submit
abstracts for poster presentation.*

Information and Application Forms

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Philadelphia, PA 19106-3483
215-440-9300 215-440-9313 (FAX)

COVER LEGEND



Pictured on this issue's cover is Anthony Cerami, previously Head of the Laboratory of Medical Biochemistry of The Rockefeller University, and now President of The Picower Institute for Medical Research of Manhasset, NY. Born in Newark, NJ, he attended Rutgers University, obtaining a B.S. degree in Agricultural Chemistry. He received his Ph.D. from The Rockefeller University, joined the faculty, and later advanced to full Professor. He was the Editor of the University's distinguished *Journal of Experimental Medicine* and, as Dean of Graduate and Post-Graduate Studies, started many innovative educational initiatives. During a professional career of almost 30 years, he has produced more than 400 papers and many patents for diagnostic tests and drugs, and he remains actively engaged in this work. He received the Luft Award in Diabetes Research of the International Diabetes Foundation, the Von Behring Award of the University of Marburg, and recently the Abbott Laboratories Award in Clinical and Diagnostic Immunology of the American Society for Microbiology. He is a member of the National Academy of Sciences (NAS) and the Institute of Medicine of the NAS. He is also an honorary member of the American Society for Clinical Investigation.

Several years ago, Dr. Cerami was offered the opportunity by philanthropists Jeffrey M. and Barbara Picower to set up a new institution. Mr. Picower is a Florida-based investor with a B.S. degree from Pennsylvania State University and a J.D. from Brooklyn Law School, and he has a particular interest in organizations specializing in medical technology. The Picower Institute for Medical Research is located in the Boas-Marks Biomedical Science Research Building of North Shore University Hospital, which is affiliated with New York University School of Medicine. The Institute has grown rapidly since its inception in 1991, reaching a present staff of over 80. It is highly productive in both publications and the discovery of potential new therapeutic and diagnostic products. Its multimillion dollar annual budget is funded by the initial Picower endowment and by research grants from government, private, and nonprofit sources.

Dr. Cerami and his groups have focused on diabetes and aging, as well as infectious diseases. With respect to diabetes,

they have investigated the chemistry of cross-linking reactions between reducing sugars (e.g., glucose) and proteins (e.g., collagen) and the dire consequences to the host of the production of these new compounds. Aminoguanidine was found to prevent this cross-linking and prevent progression of diabetic complications in experimental animal models. Phase III clinical studies are now in progress on the treatment of diabetic nephropathy with aminoguanidine.

When the Rockefeller Foundation funded Dr. Cerami to study the "great neglected diseases of mankind," he travelled to Africa, where he was intrigued by the striking emaciation (cachexia) of cattle infected with *Trypanosoma brucei*, the cause of African sleeping sickness. He soon found it to be related to a circulating macrophage protein, which induced wasting through its remarkable effects on fat and muscle metabolism. Recent Picower studies have revealed similar effects on protein catabolism and a compound that may suppress it. This circulating protein, which Dr. Cerami termed "cachectin," was found to be identical to tumor necrosis factor (TNF). Further studies showed that TNF was responsible for the lethal septic shock syndrome due to the fact that TNF was produced in large quantities by macrophages in response to bacterial endotoxins. An anti-TNF monoclonal antibody was found to prevent endotoxin-induced shock in experimental animals; it is now in clinical trials. Recently, Picower scientists have found high circulating levels of macrophage migration inhibitory factor (MIF) in the blood of animals exposed to endotoxin. This material was produced in large quantities in the pituitary gland and macrophages. As in the case of anti-TNF antibodies, shock could be prevented in animals receiving lethal amounts of endotoxin by giving anti-MIF immunoglobulins.

Turning to malaria because the parasite was becoming resistant to all available antimalarial drugs, Dr. Cerami and colleagues focused on the digestion of hemoglobin, a major nutrient of the malaria parasite. The researchers noted that heme, a degradation product of hemoglobin, was highly toxic and that the parasite had evolved a unique enzyme, heme polymerase, to sequester it into a nontoxic, insoluble pigment called hemozoin. With each cycle of the infection, RBC are lysed and the pigment released is phagocytosed by resident macrophages in the liver and spleen. These cells then release cytokines, including TNF, which may be responsible for many of the symptoms of acute malaria. Since the principal antimalarial drug, chloroquine, inhibits heme polymerase, the group is now studying the molecular basis of parasite resistance to this drug and is developing specific inhibitors of the parasite enzyme.

Two other major activities of The Picower Institute are the publication of a new scientific journal and the development of a graduate degree-granting educational program. Regarding the former, a Picower Press journal, *Molecular Medicine*, is published in cooperation with Blackwell Scientific Publishers. It has a large, international editorial board, a majority of whom are members of the U.S. National Academy of Sciences. With respect to graduate education, the Institute has been granted a charter by the Regents of the University of the State of New York to award a Ph.D. in the field of molecular medicine to young physicians dedicated to a career in medical research.

The information and photograph for this legend were kindly provided by Dr. Cerami and his staff from The Picower Institute.

Sidney Weinhouse