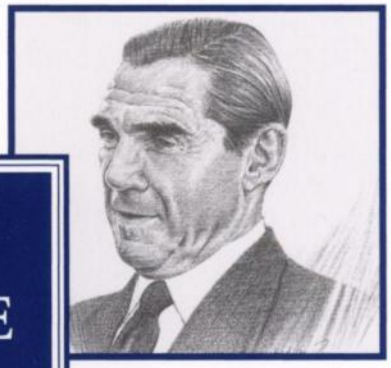
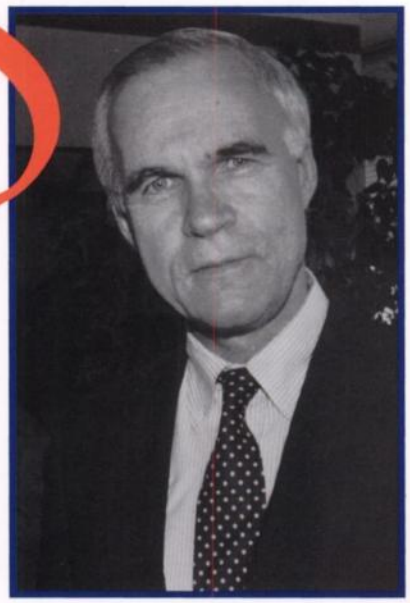
Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH



LUDWIG INSTITUTE FOR CANCER RESEARCH

THE FIRST 25 YEARS



INSIDE THIS ISSUE
Call for Abstracts for 1998 AACR Annual Meeting
Abstract Deadline: Oct. 28, 1997

October 15, 1997
Volume 57 • Number 20
PP. 4447–4665
ISSN 0008-5472 • CNREA 8

PCR ELISA Kits Simplify PCR Analysis and Quantification

Boehringer Mannheim kits provide an ideal system for genetic analysis and quantitative PCR

Method employs a standard ELISA procedure and a sequence-specific capture probe

The PCR ELISA system uses technology very similar to a standard microplate immunoassay. As detailed in Figure 1, following the PCR reaction the products are captured by an oligonucleotide probe, immobilized in a microtiter plate well, and detected using peroxidase-conjugated antibodies. The results are read using a standard microtiter plate reader.

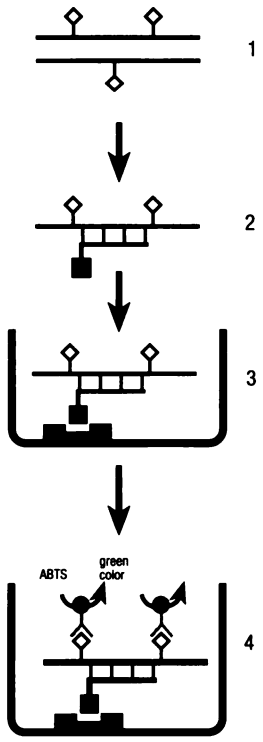


Figure 1. Principle of the PCR ELISA System. Amplification is carried out by PCR. During the reaction, digoxigenin-dUTP (⚲) is incorporated into the PCR product (step 1). An aliquot of the PCR reaction is denatured and then hybridized with a biotin-labeled oligonucleotide capture probe (┌▪) designed to anneal to an internal sequence of the PCR product (step 2). The hybridization products are immobilized on streptavidin (▬) coated microtiter plates (step 3). Peroxidase-conjugated anti-digoxigenin antibodies and ABTS® substrate are used to detect the hybrids (step 4). The colored reaction product is quantified with a microplate reader.

The PCR ELISA system provides several technical advantages compared to traditional PCR analysis methods. First, the sensitivity of ELISA detection of PCR products is 10–100 fold greater than fluorescent staining on agarose gels. Second, the use of a capture probe provides verification of the authenticity of the PCR reaction product. And third, the use of an ELISA format affords rapid analysis of multiple PCR reactions simultaneously.

Capture probe technology allows precise characterization of the sequence of PCR products

Many current PCR applications such as HLA genotyping, the analysis of microorganisms in biological samples, and the detection of specific gene mutations require precise verification of PCR product specificity. Because the PCR ELISA system utilizes a sequence-specific capture probe, it can easily be adapted to these protocols by simply varying the nucleotide sequence of the capture probe to correspond to the desired target sequence. Discrimination of point mutations can be readily accomplished by modifying the stringency of the probe hybridization and washings conditions (Figure 2).

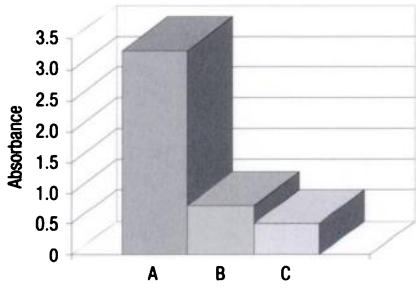


Figure 2. Discrimination of Single Base Mismatches. Three 20-mer capture probes were hybridized to actin gene PCR products. One probe perfectly matched the expected sequence (A) and the other two contained different single base pair mismatches (B, C). Hybridization at 55°C demonstrated specific binding of only the perfectly matched oligonucleotide probe.

Quantitative PCR assays are simple and affordable

Quantitative PCR studies require the analysis of multiple PCR reactions. Traditional methods for quantitative PCR analysis are laborious or involve the purchase of complicated expensive equipment. Boehringer Mannheim's PCR ELISA system provides a simple affordable alternative. The PCR ELISA system allows multiple samples to be processed in parallel in standard 96-well microtiter plates. Multichannel pipettors and a standard microplate reader is all that is required to obtain accurate reliable quantitative PCR results. If fewer than 96 wells are required, the microtiter plates can be readily separated into 8-well strips to allow for economical use of the kit components.

A complete system of PCR ELISA kits is now available

Three kits comprising the PCR ELISA system are available from Boehringer Mannheim. Choose one of two labeling kits, in combination with the PCR ELISA Detection Kit, to fit the needs of your experiments (Table 1). Order the PCR ELISA system from your local Boehringer Mannheim representative or, for more information, visit our internet web site at http://biochem.boehringer-mannheim.com.

Product	Cat. No.
PCR ELISA (DIG Labeling)*	1 636 120
PCR ELISA DIG Labeling^{PLUS}†	1 835 297
PCR ELISA (DIG Detection)†	1 636 111

Table 1.

* This product is accompanied by a limited license to use it in the Polymerase Chain Reaction (PCR) process for life science research in conjunction with a thermal cycler whose use in the automated performance of the PCR process is covered by the up-front license fee, either by payment to Perkin-Elmer or as purchased, i.e., an authorized thermal cycler.

† This product is sold under licensing arrangements with Roche Molecular Systems and The Perkin-Elmer Corporation.

ABTS® is a registered trademark of Boehringer Mannheim.

Helping biomedical research become medical practice.

BOEHRINGER MANNHEIM

mannheim boehringer

National Cancer Institute
Division of Basic Sciences
Bethesda, Maryland

Opening Date: September 22, 1997
Closing Date: November 10, 1997

Announcement Number: CA-97-0328

Director, Division of Basic Sciences

The National Cancer Institute (NCI), National Institutes of Health (NIH) has recently taken major steps to assure the continuation of innovative biomedical research that meets the scientific standards of the research community. In order to further this objective and assure its success, the NCI is seeking an outstanding senior-level scientist to fill the position of Director, Division of Basic Sciences (DBS). The Director, DBS provides scientific leadership of NCI's intramural basic research program, initiating and coordinating scientific programs that encourage the effective recruitment of key research staff to generate innovative investigator-initiated research. The Director is responsible for creating and maintaining a research environment that fosters collaboration between NCI's intramural research investigators and extramural scientists and continually stimulates novel research directed ultimately towards the treatment and prevention of cancer, AIDS and other related diseases. The Director, DBS is also responsible for establishing effective partnerships with academia and industry to assure that innovative technology is developed and is successfully transferred, enhanced, and commercialized. The Director determines immediate and long-range research objectives and directs the implementation of these objectives through the effective utilization of fiscal and other resources. Long-term planning includes expanded research efforts into the areas of developmental biology, cell biology, and molecular cytogenetics as well as the maintenance of innovative, ongoing basic research. The Director must ensure that DBS research reflects the highest standards of scientific excellence validated through rigorous peer review. The Director, DBS will provide national and international leadership to ensure that the quality of biomedical research in DBS enhances the position of the organization as a world leader in the cancer research field.

The DBS is organized into 34 Laboratories and Branches staffed with approximately 700 personnel positions and 500 Fellowship positions supported with an annual budget of approximately $125 million. Candidates should be internationally recognized for their scientific accomplishments, leadership and collaborative capabilities in the areas of molecular biology, cell biology, genetics, immunology, biochemistry and/or other areas of basic studies of cancer, AIDS and related diseases and the application of modern biotechnology to these studies. Candidates must also possess a medical and/or other doctoral-level degree in a biomedical or related field. In addition, candidates must be either a U.S. citizen, a citizen of a treaty-allied country, or a nonresident alien with a valid work visa. Total annual compensation will be commensurate with education and experience and range from $75,935 to $148,400.

Applicants should send a letter expressing their interest in the position; a statement of research interests; a career synopsis and brief biography; curriculum vitae and bibliography; and the names and addresses of five individuals who can be contacted as references. Letters of reference should not be submitted by the applicant. This material should be sent to:

Ms. Toni McKeown
National Cancer Institute
Human Resources Management and Consulting Branch
6120 Executive Boulevard
Room 550, EPS
Rockville, MD 20852

Applications may also be faxed to (301) 402-9333.

If you need additional information, please call Ms. Toni McKeown, NCI Human Resources Management and Consulting Branch on (301) 402-2812.

Selection for this position will be based solely on merit, with no discrimination for non-merit reasons such as race, color, gender, national origin, age, religion, sexual orientation, or physical or mental disability.

NCI IS AN EQUAL OPPORTUNITY EMPLOYER

AACR SPECIAL CONFERENCE IN CANCER RESEARCH

Angiogenesis and Cancer

January 24-28, 1998
Hyatt Orlando
Orlando, FL

CONFERENCE CO-CHAIRPERSONS

Judah Folkman / Boston, MA
Michael Klagsbrun / Boston, MA

CONFERENCE PROGRAM

Keynote Address
Nicole Le Douarin / Nogent sur Marne, France

Blood Vessels and Development
Patricia D'Amore / Boston, MA
Donald E. Ingber / Boston, MA
Jeffrey M. Isner / Boston, MA

Mechanisms of Vasculogenesis and Angiogenesis
Werner Risau / Bad Nauheim, Germany
Peter Carmeliet / Leuven, Belgium
Douglas Hanahan / San Francisco, CA

VEGF and VEGF Receptors
Kari K. Alitalo / Helsinki, Finland
Harold F. Dvorak / Boston, MA
Napoleone Ferrara / S. San Francisco, CA
Kenneth A. Thomas / West Point, PA

Angiopoietin and TIE Receptors
George D. Yancopoulos / Tarrytown, NY
Bjorn R. Olsen / Boston, MA

Tumor Angiogenesis and Metastasis
Rakesh K. Jain / Boston, MA
Robert S. Kerbel / Toronto, Ontario, Canada
Isaiah J. Fidler / Houston, TX
Ann F. Chambers / London, Ontario, Canada

Inhibitors of Angiogenesis
Luisa Iruela-Arispe / Boston, MA
Noël Bouck / Chicago, IL
David A. Cheresh / La Jolla, CA

Clinical Applications
Noel Weidner / San Francisco, CA
Judah Folkman / Boston, MA

Additional Speakers to be Announced

Application Deadline: October 13, 1997

Information and Application Forms:
American Association for Cancer Research
Public Ledger Building, Suite 826
150 South Independence Mall West
Philadelphia, PA 19106-3483
215-440-9300 215-440-9313 (FAX)
E-mail: aacr@aacr.org
Website: http://www.aacr.org

AACR SPECIAL CONFERENCE IN CANCER RESEARCH

Molecular Mechanisms of Apoptosis Regulation

January 9-13, 1998
Renaissance Esmeralda Resort
Indian Wells (Palm Springs), CA

CONFERENCE CO-CHAIRPERSONS

John C. Reed / La Jolla, CA
Vishva M. Dixit / S. San Francisco, CA

PROGRAM COMMITTEE

Douglas R. Green / La Jolla, CA
Hermann Steller / Cambridge, MA
Guido Kroemer / Villejuif, France
David L. Vaux / Melbourne, Australia

CONFERENCE PROGRAM

Cell Death Receptors
Vishva M. Dixit / S. San Francisco, CA
Peter H. Krammer / Heidelberg, Germany
Jurg Tschopp / Lausanne, Switzerland
Dale Bredesen / La Jolla, CA

Cell Death Proteases
R. Chris Bleackley / Edmonton, Alberta, Canada
Arnold H. Greenberg / Winnipeg, Manitoba, Canada
Guy Salvesen / La Jolla, CA
Yuri Lazebnik / Cold Spring Harbor, NY
Donald W. Nicholson / Montreal, Quebec, Canada
Emad S. Alnemri / Philadelphia, PA
Junying Yuan / Cambridge, MA

Bcl-2 Family Proteins: Mechanisms of Action
Yoshihide Tsujimoto / Osaka, Japan
Stanley J. Korsmeyer / St. Louis, MO
Robin Brown / London, England
John C. Reed / La Jolla, CA
Andreas Strasser / Melbourne, Australia

Mitochondria, Cytochrome C, and Cell Death
Guido Kroemer / Villejuif, France
Xiaodong Wang / Dallas, TX
Douglas R. Green / La Jolla, CA

Stress Responses and Cell Death Control
Richard N. Kolesnick / New York, NY
Yusuf A. Hannun / Durham, NC
Eileen P. White / Piscataway, NJ
Michael E. Greenberg / Boston, MA

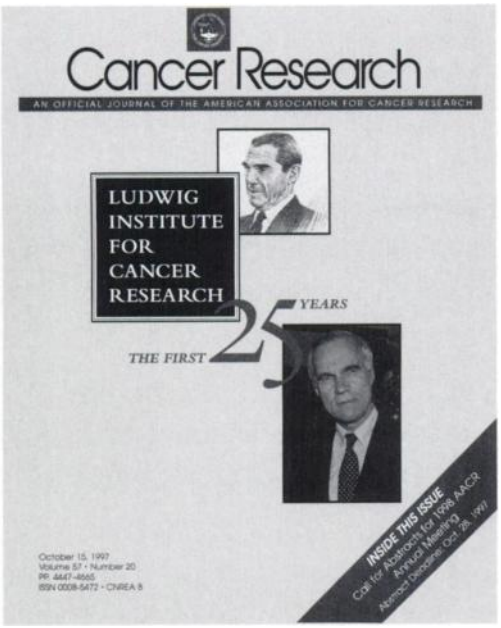
Genetics of Cell Death Regulation: New Insights into the Cell Death Pathway
Hermann Steller / Cambridge, MA
Michael O. Hengartner / Cold Spring Harbor, NY
John M. Abrams / Dallas, TX

IAP Family Proteins
David L. Vaux / Melbourne, Australia
Alex Mackenzie / Ottawa, Ontario, Canada
Lois K. Miller / Athens, GA

Application Deadline: October 20, 1997

Information and Application Forms:
American Association for Cancer Research
Public Ledger Building, Suite 826
150 South Independence Mall West
Philadelphia, PA 19106-3483
215-440-9300 215-440-9313 (FAX)
E-mail: aacr@aacr.org
Website: http://www.aacr.org

COVER LEGEND



Organized in 1971, the Ludwig Institute for Cancer Research carries on a global research effort with a staff of over 600. The Institute was established by Daniel K. Ludwig (*top*), one of the preeminent figures in the shipping industry, who died in 1992 at the age of 95. In his founding statement, Mr. Ludwig clearly articulated the principles that have guided the development of the Lugwig Institute: "Success in any complex enterprise consists in bringing the best minds to bear on each problem, in providing the best resources possible, and in putting each concept into practice whenever and wherever the opportunities are most favorable. I believe firmly in the value of applying these principles in grappling with tasks as momentous as finding ways to relieve the human suffering caused by cancer."

The research of the Institute is conducted through multiple Branches rather than at a single site. This model was chosen to facilitate the worldwide recruitment of scientists and to draw on the strengths of a variety of different laboratory and clinical environments. The Branches are situated at major research and hospital centers, and through collaborations, teaching activities, and clinical programs, the Branches have become an integral part of the academic life at each of the host institutions.

Each Branch focuses on a program of research defined by the Branch Director in relation to the overall objectives of the Institute. The number of staff at each Branch is intended to be sufficient to enable the Branch Directors to address complex biological problems related to cancer with a critical mass of interactive scientists having expertise in several scientific disciplines. The quality of research is monitored on an ongoing basis by the Institute's Scientific Committee (Walter Bodmer, Samuel Hellman, George Klein, Arthur Pardee, and Harald zur Hausen) and by a process of external peer review.

Branches of the Institute are: Brussels Branch of Human Cancer Cell Genetics, Director: Thierry Boon; Lausanne Branch of Immunology, Director: Jean-Charles Cerottini; London (St Mary's) Branch of Molecular Virology, Director: Paul J. Farrell; London (University College) Branch of Cell and Molecular Biology, Director: Michael D. Waterfield; Melbourne Branch of Tumor Biology, Director: Antony W. Burgess; New York Branch of Human Cancer Immunology, Director: Lloyd J. Old; San Diego Branch of Cancer Genetics, Director: Webster K. Cavenee; Sao Paulo Branch of Cancer Biology and Epidemiology, Director: Ricardo R. Brentani; Stockholm Branch of Molecular and Cell Biology, Director: Ralf E. Pettersson; and Uppsala Branch of Growth Regulation, Director, Carl-Henrik Heldin.

In addition to the ten Branches in seven countries, a growing number of collaborations and affiliations with laboratory and clinical investigators at other institutions around the world are being established. These are intended to complement and extend the Institute's research programs. Additional collaborations are also anticipated as a consequence of another gift of Mr. Ludwig to the academic community: establishment of the Virginia and D. K. Ludwig Chairs and Programs in Cancer Research at six distinguished academic centers in the United States (Harvard, MIT, University of Chicago, Johns Hopkins, Stanford, and Memorial Sloan-Kettering Cancer Center). The establishment of the Institute and the Ludwig Chairs and Programs provides the structure and the resources to pursue Mr. Ludwig's vision of an interactive and global research effort to combat cancer.

To explore the clinical potential of its research findings, the Institute has developed a Clinical Trials Program over the past five years. Currently, 17 Ludwig-sponsored Phase I/II trials of vaccine-based or antibody-based therapies are ongoing or about to begin at academic centers in 11 countries. The trials are reviewed and approved by the Institute's Protocol Review Committee (Chairman, H. F. Oettgen) and managed by the Institute's Office of Clinical Trials Management. To provide investigational agents for clinical trials, the Institute has constructed a GMP production facility at the Melbourne Branch. The development of the Clinical Trials Program reflects a strong commitment of the Institute to facilitate and participate in the translation of laboratory findings into clinical therapies. It is the Institute's conviction that Phase I/II trials represent the last stage of the initial discovery process, not the first stage of a new process, and that the significance of a new discovery in cancer is not known until its clinical impact has been established.

The Director and CEO of the Ludwig Institute is Lloyd J. Old (*bottom*). He was born in San Francisco, CA, and received his M.D. degree from the University of California, San Francisco, in 1958. After completing postdoctoral work, he joined the staff of Memorial Sloan-Kettering Cancer Center, became a Member in 1968, and from 1973 to 1983 served as Associate Director of Research. Dr. Old was one of the founding members of the Scientific Committee of the Ludwig Institute (with Hugh Butt, Henri Isliker, and Carl Baker) and became Director of the Institute in 1988. Dr. Old's research contributions over the past three decades have established many of the principles and priorities of modern tumor immunology. In earlier work, he and his colleagues introduced BCG to tumor immunotherapy, discovered the first link between the Major Histocompatibility Complex and disease (leukemia), found the unexpected association between EBV and nasopharyngeal carcinoma, discovered TNF, defined the concept of cell surface differentiation antigens with the discovery of TL, Lyt-2 (CD8), and a range of other mouse antigenic systems of viral and nonviral origin, codiscovered p53 with two other groups, and identified the tumor immunogenicity of heat shock protein gp96. Over the past fifteen years, Dr. Old and his coworkers have performed a detailed serologic dissection of the cell surface antigenic structure of human cancers recognized by mouse and human antibodies and have defined an extensive list of new antigenic targets for antibody-based and vaccine-based therapies, leading to the clinical testing of five antibodies his group developed and the ongoing clinical trials of GM2 vaccines for melanoma. Dr. Old is the Director of the Scientific Advisory Council of the Cancer Research Institute, an organization that provides support for Fellows and Investigators in the field of immunology and cancer immunology. He organizes and chairs the annual CRI Symposia series on Cancer Immunotherapy. Dr. Old is the author or co-author of 500 publications and is a member of the National Academy of Sciences.

Dr. Old has been a member of the American Association for Cancer Research (AACR) since 1962, and he was elected to Honorary Membership in 1995. He has served with distinction in Association activities, including a term on the Board of Directors from 1980–83 and service on the Awards Committee from 1980–82 and the Special Memberships Committee in 1981. Also, he helped organize the 1990 AACR Special Conference, "The Molecular Basis of Tumor Immunology," serving as a member of its Program Committee. In addition, he was the recipient of the G. H. A. Clowes Memorial Award at the 1980 AACR Annual Meeting.

Sidney Weinhouse