Clinical Cancer Research
An Official Journal of the American Association for Cancer Research

SCOPE
Clinical Cancer Research, a new journal of the American Association for Cancer Research (AACR), publishes original articles describing clinical research on the cellular and molecular characterization, prevention, diagnosis, and therapy of human cancer. Its focus is on innovative clinical research and translational research which bridges the laboratory and the clinic. Clinical Cancer Research is especially interested in clinical trials evaluating new treatments for cancer; research on molecular abnormalities that predict incidence, response to therapy, and outcome; and laboratory studies of new drugs and biological agents that will lead to clinical trials in patients.

SPECIFIC AREAS OF INTEREST

CLINICAL AND TRANSLATIONAL RESEARCH IN:
- Molecular pharmacology and chemotherapy
- Drug sensitivity and resistance
- Tumor immunology and immunotherapy
- Radiobiology and radiation oncology
- Solid tumor oncology
- Hematological malignancies
- Surgical oncology
- Pediatric oncology
- Molecular oncology and cancer genes
- Pathology, markers, and prognostic indicators
- Growth factors, cytokines, and signal transduction
- Bone marrow transplantation
- Gene therapy
- Cancer endocrinology
- Cell adhesion, invasion, and metastasis
- Prevention of primary and recurrent cancer
- Differentiation and cell death
- Clinical genetics
- Detection of minimal disease

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Department of Medicine
Memorial Sloan-Kettering Cancer Center
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The annual dues of active members of the American Association for Cancer Research are $160, $40 of which may be applied to a subscription to Clinical Cancer Research. Corresponding members of the Association will be charged an appropriate fee to offset second-class postage costs. Payment of dues and changes of address of members of the Association should be sent promptly to Margaret Foti, Executive Director, American Association for Cancer Research, Public Ledger Bldg., Suite 816, 150 South Independence Mall West, Philadelphia, PA 19106-3483; Telephone: (215) 440-9300; FAX: (215) 440-9313.

Submission of Manuscripts
Clinical Cancer Research, a new journal of the American Association for Cancer Research, publishes original articles describing clinical research on the cellular and molecular characterization, prevention, diagnosis, and therapy of human cancer. Its focus is on innovative clinical research and translational research which bridges the laboratory and the clinic. Clinical Cancer Research is especially interested in clinical trials evaluating new treatments for cancer; research on molecular abnormalities that predict incidence, response to therapy, and outcome; and laboratory studies of new drugs and biological agents that will lead to clinical trials in patients. All submissions undergo peer review. Papers should be sent to John Mendelsohn, M.D., Editor-in-Chief, Clinical Cancer Research, Department of Medicine, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10021; Telephone: (212) 639-5878; FAX: (212) 772-8375.

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Four educational sessions will be offered simultaneously during the upcoming annual meeting. A registration fee of US$35 or C$50 for members and predoctoral students, and US$50 or C$72 for nonmembers will be charged. The intent of these sessions is to provide an overview of an important area of cancer research for scientists who are not specialists in the area. Speakers have been asked to cover all significant developments in the fields. Registrants in each session will receive a syllabus including a selected bibliography of highly relevant articles.

**Educational Session 1**

**Molecular Modeling to Medical Monitoring: The Development of New Anticancer Agents**

**Chairperson**

**DANIEL D. VON HOFF.** Cancer Therapy and Research Center, San Antonio, TX.

Elegant basic cancer research frequently culminates in the development of a potentially therapeutic agent. However, an incomplete understanding of the difficulties in carrying a new therapeutic agent from the bench to the bedside frequently results in a tremendous slowing down of the drug development process. Currently, the time it takes to develop a new anticancer drug is approximately seven years from the time it is conceived until the first trial in patients (the IND), plus an additional seven years from the time the first patient is treated until the drug is approved by regulatory agencies.

The purpose of this educational session is to educate attendees on what preclinical work is necessary to obtain an IND for the first clinical trial in patients. A second part of the session will deal with special problems in the design of clinical trials including Phase I, Phase II, and Phase III studies. Discussions will center around agents which are particularly difficult to develop (such as angiogenesis inhibitors or differentiating agents). Finally, the development of agents for prevention -- a particularly challenging area of clinical trials research -- will be discussed. It is hoped that attendees will emerge from the session with a greater understanding of the steps necessary for the translation of a basic science finding from the bench to the bedside.

**Program**

**Overview.** Daniel D. Von Hoff.

What Is Really Necessary for Beginning a Trial with a New Agent in Patients? **David Ross Parkinson,** National Cancer Institute, Bethesda, MD.

Special Problems in the Design of Clinical Trials. **Daniel D. Von Hoff.**

Clinical Trials with Prevention Agents. **David S. Alberts,** University of Arizona Cancer Center, Tucson, AZ.

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**Educational Session 2**

**Gene Therapy**

**Chairperson**

**ALBERT B. DEISSEROTH,** UT M.D. Anderson Cancer Center, Houston, TX.

Current approaches to the use of genetic modification of somatic cells for the treatment of cancer will be reviewed including: genetic chemoprotection (to protect the normal hematopoietic cells from chemotherapy induced myelosuppression); recombinant anticancer vaccines; adenoviral vectors for cancer therapy; and molecular immunoenhancement therapy for cancer.

**Program**

Recombinant Vaccines for Cancer Therapy. **Jeffrey Schlom,** National Cancer Institute, Bethesda, MD.

Genetic Chemoprotection for Cancer and Gene Therapy. **Albert B. Deisseroth.**

Genetic Immunoenhancement for Gene Therapy. **Gary Nabel,** University of Michigan Medical Center, Ann Arbor, MI.

Adenoviruses in Genetic Therapy. **Ronald Crystal,** Cornell University Medical College, New York, NY.
Educational Session 3
Genetic Instability in Cancer

Chairperson
LAWRENCE A. LOEB. University of Washington School of Medicine, Seattle, WA.

Deficits in DNA repair have recently been firmly associated with both inherited and sporadic human cancers. The enzymes have been appointed as "molecules of the year". We will consider the recent reports on multiple mutations in cancer, the relationship of altered DNA repair to microsatellite instability, the occurrence of microsatellite instability in inherited human colon cancer, and the reports on microsatellite instability in both sporadic malignancies and premalignant diseases. Emphasis in this session will be on methods, clinical implications, hands-on assays, and prognostic implications.

Program
Multiple Mutations in Cancer. Lawrence A. Loeb.
DNA Replication, Fidelity, and Mismatch Repair in Cancer. Thomas A. Kunkel. N.I.E.H.S., Research Triangle Park, NC.
Defective Mismatch Repair in Colorectal Cancer. C. Richard Boland. University of Michigan, Ann Arbor, MI.
Microsatellite Instability in Pancreatic Cancer and Non-Hereditary Colon Cancer. Teri Brentnall, University of Washington, Seattle, WA.

Educational Session 4
Cytochrome P450

Chairperson
COLIN R. JEFCOATE, University of Wisconsin, Madison, WI.

An understanding of the cytochrome P450 subfamily of genes is important to several areas of cancer research including tumor biology, carcinogenesis, pharmacology, and therapeutics. This session will explore the many facets of Cytochrome P450 and its implications for future research. It will be of interest to both basic and clinical scientists in the field.

Program
Overview of Cytochrome P450. Colin R. Jefcoate.
Human Polymorphisms, Drug Metabolism, and Chemotherapy. F. Peter Guengerich. Vanderbilt University School of Medicine, Nashville, TN.
The Role of Cytochrome P450 in Target Tissues as an Activator of Carcinogens. John J. Reiners, Jr., Wayne State University, Detroit, MI.
METHODS WORKSHOPS
86TH AACR ANNUAL MEETING
Saturday, March 18, 1995, 2:00-6:00 p.m.

Two state-of-the-art methods workshops will be offered simultaneously during the upcoming annual meeting. A registration fee of US$35 or C$50 for members and predoctoral students, and US$50 or C$72 for nonmembers will be charged. The intent of these sessions is to provide a detailed description of new research techniques and to illustrate their potential for cancer research. Registrants in each session will receive a syllabus including a selected bibliography of highly relevant articles.

Methods Workshop 1
General, In Situ, and Quantitative PCR

Chairperson
SARASWATI SUKUMAR, Johns Hopkins School of Medicine, Baltimore, MD

The advent of PCR has revolutionized the field of cancer by facilitating genetic analysis of the scantiest resources of fresh as well as archival tissue material. Human tumors are comprised of heterogeneous mixtures of different cell populations, many of which represent past steps in tumor progression. Therefore the identification of mutations in specific cell types and topographic locations can provide information on the timing of events in tumor progression and growth.

Selective ultraviolet radiation fractionation (SURF), using UV to destroy the DNA present in undesirable cells, facilitates the microdissection of fixed tissue specimens. Information is obtained not only on the presence of a mutation, but also the specific types of cells which harbor the mutation. Differential display was developed as a tool for comparative studies at the level of mRNA expression in eukaryotic cells. A comparison of mRNA species from the same tissue origin, such as the normal and tumor cells, allows identification of both up- and down-regulated genes of interest. The genetic suppressor element technology allows the identification of novel genes and their functions as well as the discovery of new functions for known genes through targeted gene inactivation or down modulation. Identification of new suppressor genes, genes associated with drug resistance, genes supporting pathogenic viruses, and apoptotic genes are some applications of this method. Finally, fine structure analysis for altered genes requires a battery of tests based on allele-specific detection of mutations in oncogenes, tumor suppressor genes, and imprinted genes. PCR-based methods that allow the detection of incipient tumors and minimal residual disease will be discussed.

Registrants should have prior knowledge and experience with the PCR technique. Written material will be given to each attendee that provides detailed protocols and troubleshooting advice. The specific techniques to be discussed are particularly useful in pathology and the genetic analysis of tumors.

Program
Direct Analysis of Human Tumor Progression with Selective Ultraviolet Radiation Fractionation: Back to the Future. Darryl Shibata, University of Southern California, Los Angeles, CA.
Genetic Suppressor Elements as a Tool for Gene Identification. Tatyana Holzmayer, Ingenex, Menlo Park, CA.
Analysis of Altered Gene Expression in Cancer by Differential Display. Peng Liang, Dana-Farber Cancer Institute, Boston, MA.
Allele-Specific Detection of Mutated Oncogenes and Tumor Suppressor Genes. Saraswati Sukumar.

Methods Workshop 2
Gene Targeting and Gene Trapping in Mice

Chairpersons
ANDRAS NAGY, Mount Sinai Hospital, Toronto, Canada
JANET ROSSANT, Mount Sinai Hospital, Toronto, Canada

The ability to manipulate the mammalian genome by means of introducing genetic alterations into mouse embryonic stem (ES) cells and hence into mice, has revolutionized the genetic analysis of biological processes including cancer. In this workshop, the technology of targeted mutagenesis as well as the techniques required to manipulate ES cells and make mouse chimeras will be described in detail. Novel approaches to generate site-specific and tissue-specific targeted mutations will be described, as well as methodologies to identify and mutate novel genes using gene trap vectors.

Program
Gene Targeting in Embryonic Stem Cells. Ramiro Ramirez-Solis, Texas A & M University, Houston, TX.
ES Cells, Making Chimeras, and Analyzing Embryos. Richard Behringer, M. D. Anderson Hospital, Houston, TX.
Capturing Genes Important in Mouse Development. William Skarnes, The University of Edinburgh, Edinburgh, Scotland.
REGISTRATION FORM
METHODS WORKSHOPS AND EDUCATIONAL SESSIONS

PLEASE TYPE OR PRINT INFORMATION REQUESTED BELOW
Persons wishing to attend a methods workshop or educational session must be registered for the AACR Annual Meeting and must pay an additional fee of US$35 or CS$50 for members and predoctoral students, and US$50 or CS$72 for nonmembers.

1. SELECT SESSION: Check the box next to the one methods workshop or educational session you wish to attend. You may attend only the session for which you are registered.

☐ Methods Workshop 1: General In Situ, and Quantitative PCR. Saraswati Sukumar, Chairperson. (Note: If you check this box, please complete Section 5 below as well.)

☐ Methods Workshop 2: Gene Targeting and Gene Trapping in Mice. Janet Rossand and Andras Nagy, Chairpersons. (Note: If you check this box, please complete Section 6 below as well.)


☐ Educational Session 2: Gene Therapy. Albert B. Deisseroth, Chairperson.

☐ Educational Session 3: Genetic Instability in Cancer. Lawrence A. Loeb, Chairperson.

☐ Educational Session 4: Cytochrome P450. Colin R. Jeffcoat, Chairperson.

2. NAME: ____________________________________________
   Last First M.I.

3. ADDRESS: ____________________________________________
   Institution
   Street, Building, or P.O. Box
   City State or Province Postal Code
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4. REGISTRATION STATUS (Check 1): ___ I have already registered for the AACR Annual Meeting.
   ___ My Annual Meeting Registration Form is enclosed.

5. SUPPLEMENTAL QUESTIONS FOR REGISTRANTS FOR METHODS WORKSHOP 1 ONLY:
   A. Do you routinely use the PCR technique? ___ Yes ___ No
   B. Are you a pathologist interested in genetic analysis? ___ Yes ___ No
   C. Do you have prior gene cloning experience? ___ Yes ___ No
   D. Do you intend to use the techniques described in this workshop in the near future? ___ Yes ___ No

6. SUPPLEMENTAL QUESTIONS FOR REGISTRANTS FOR METHODS WORKSHOP 2 ONLY:
   A. Do you have hands-on experience with any of the following:
      i. culturing mouse embryonic stem cells ___ Yes ___ No
      ii. generating mouse chimeras ___ Yes ___ No
      iii. design of targeted mutagenesis vectors ___ Yes ___ No
   B. What is the current status of ES cell/mutagenesis technology in your lab? (Check only 1)
      ___ ongoing, active, and successful ___ in initial stages of establishment ___ not yet part of my program
   C. What are the areas in which you most need practical information? (Check as many as apply.)
      ___ how to make standard targeted mutations ___ how to culture ES cells
      ___ how to analyze embryonic mutant phenotypes ___ how to make chimeras
      ___ how to develop more specific targeted mutations ___ how to use ES cells to find and mutate novel genes
      ___ other (specify) ____________________________

THE DEADLINE FOR REGISTRATION BY MAIL IS FEBRUARY 17, 1995
If space permits, registrations will be accepted after this date and at the annual meeting.

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