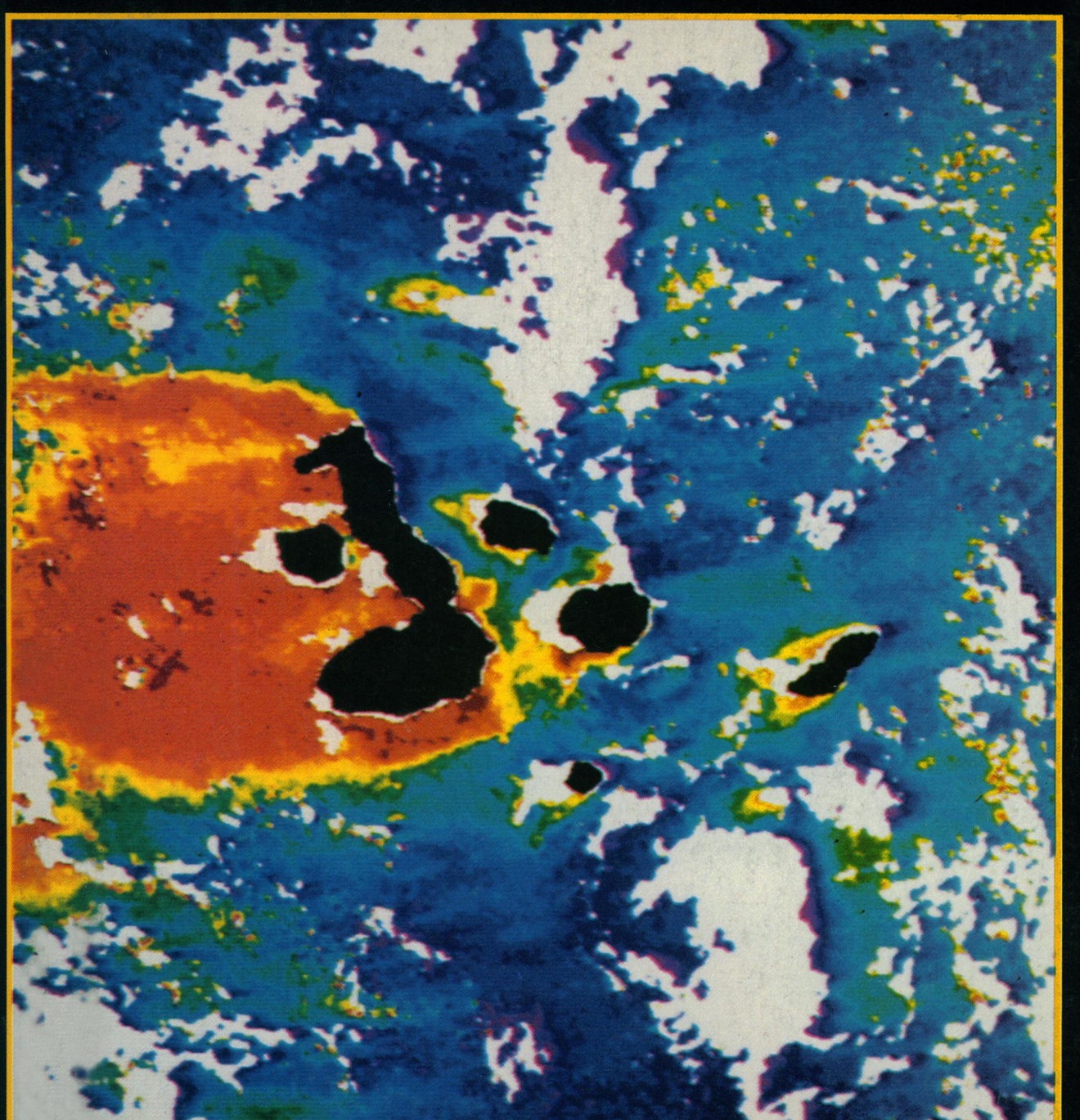
30 November 1984 • Vol. 226 • No. 4678 $2.50

SCIENCE

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



Cambridge World of Science

Beyond the sterile world of laboratories is a mysterious world that formulae cannot explain and the mind but dimly imagine. It is a world of awesome spectacle – a scarlet flare blazing 300,000 km above the sun – and microscopic wonder.

The beautiful books in the *Cambridge World of Science* probe these mysteries, unraveling their complexities, celebrating their splendor.

We invite you to visit your bookstore, page through these books, and explore the *Cambridge World of Science*.

OUR GREEN AND LIVING WORLD
The Wisdom to Save It
Edward S. Ayensu, et. al.
A remarkable exploration of man's use of plants throughout the world, written with a concern for global conservation.
Over 300 color illus.
8½ x 11 *$24.95*

THE CAMBRIDGE GUIDE TO THE MATERIAL WORLD
Rodney Cotterill
A beautiful and accessible guide to all the materials in our world, both physical and biological.
190 plates
8¼ x 11⅛ *$34.50*

SECRETS OF THE SUN
The late Ronald Giovanelli
This startling and authoritative book describes all the main activities that occur on or in the sun.
63 plates
7½ x 9⅛ *$19.95*

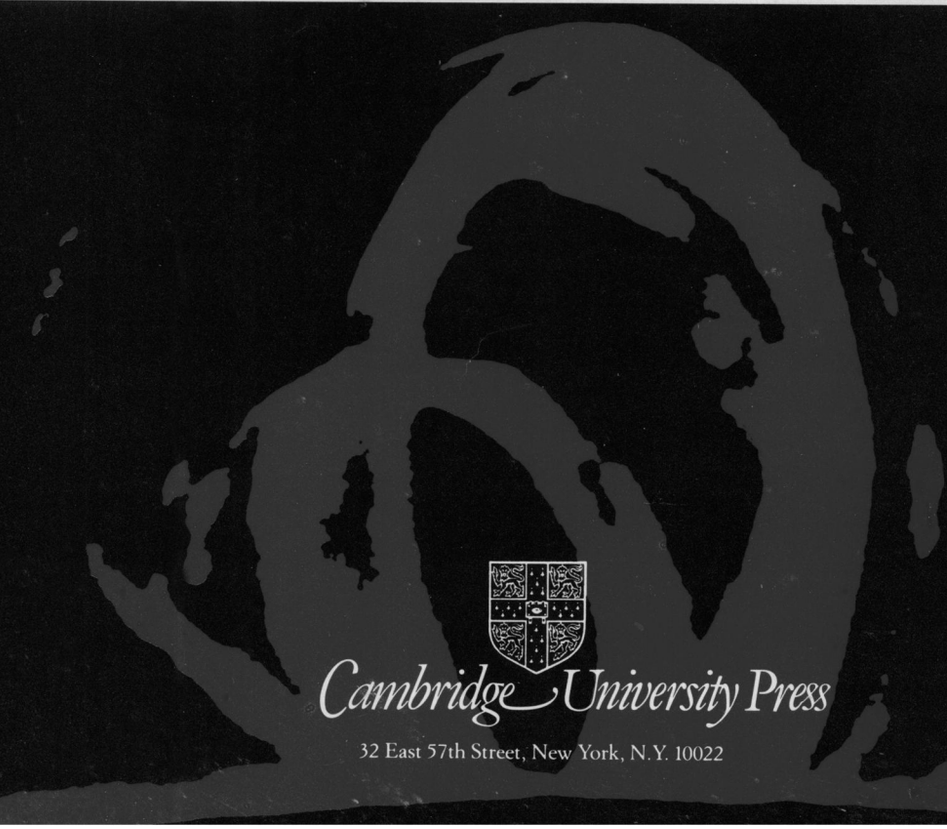
THE NEW ASTRONOMY
Nigel Henbest and Michael Marten
The most spectacular views of the night sky taken from the latest technologies in astronomy. "...a truly fascinating book." – *UPI*
Over 250 illustrations
8¼ x 11⅛ *$24.95*

CREATIVE COMPUTER GRAPHICS
Annabel Jankel and Rocky Morton
This celebration of the stunning images created by computer technology tells how they are made and used.
200 illustrations
11½ x 11½ *$29.95*

SPACELAB
Science in Earth Orbit
David Shapland and Michael Rycroft
Foreword by James M. Beggs.
The story of Spacelab, its development, goals, experiments, and crew.
Many illustrations
7⅛ x 9¼ *$22.50*

COLOURS OF THE STARS
David Malin and Paul Murdin
Two celebrated scientists explain why celestial bodies appear in a variety of colors.
130 photographs
8⅝ x 11 *$27.95*

Available at bookstores or by telephone order. Call (outside New York State and Canada) **1-800-431-1580. MasterCard/VISA** *accepted.*



Cambridge University Press

32 East 57th Street, New York, N.Y. 10022

THE SECOND ANNUAL CONGRESS FOR

AUTOMATION, SCALE-UP and the ECONOMICS OF BIOLOGICAL PROCESS ENGINEERING

FEBRUARY 7-8, 1985
SAN FRANCISCO HILTON, SAN FRANCISCO, CALIFORNIA

A one and one half day congress following:
THE FIFTH ANNUAL CONGRESS FOR RECOMBINANT DNA RESEARCH
THE FOURTH ANNUAL CONGRESS FOR HYBRIDOMA RESEARCH

ORGANIZED BY **SCHERAGO ASSOCIATES, INC.**
in conjunction with **GENETIC ENGINEERING NEWS**

CHAIRMAN: Gerald L. Hawk, PhD, Zymark Corporation

TOPICS:

Cell Bank Characterization for Recombinant DNA Mammalian Cell Lines: Implications for Process Development.

Cell-Free Translation of Recombinant RNA: a Feasibility Assessment.

Feasible and Optimal Retrofitting of Soluble Enzyme Batch Processes to Immobilized Enzyme Processes.

Considerations for the use of Genetically Engineered Mammalian Cell Cultures for the production of Biologicals.

Laboratory Automation and Robotics in Bio-Technology.

Automation and Scale-up of Chromatographic Protein Purification.

Single Step Purification of Monoclonal Antibodies by Anion Exchange High Performance Liquid Chromatography.

Membrane Process Systems for Protein Seperations.

Large scale Culture of Animal Cells using the Opticell™ System.

Large scale production of Monoclonal Antibodies, utilizing the Encapcel™ System.

The role of the Entrepreneur in Bio-Technology.

Trends in Government Regulation and Voluntary Standardization in Bio-Technology.

Large scale production of Monoclonal Antibodies and their use for Immunopurification.

Entrapping Hybridoma Cells in a Membrane-Based Perfusion System increases antibody production.

Use of Automated Hollow-Fiber Technology for Economical Production of Monoclonal Antibodies.

Hollow Fiber Cell Culture for Cell-Product manufacturing.

Plasma Protein Fractionation and Purification by Zeta-Prep Ion Exchange Cartridge.

Registration Fee: $300.00
Attendance will be limited. Make checks payable to: **Scherago Assoc., Inc.**

☐ Please reserve _____ space(s): Registration Fee must be included.
☐ Please send Registration Application.
Cancellations must be received by January 9, 1985.

Name _____

Dept. _____

Organization _____

Street _____

City _____ State _____ Zip _____

Telephone: (___) _____

Return to:
Automation, Scale-Up; c/o Scherago Associates, Inc.
1515 Broadway, New York, NY 10036 • (212) 730-1050

ISSN 0036-8075

30 November 1984

Volume 226, No. 4678

SCIENCE

SCIENCE is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1515 Massachusetts Avenue, NW, Washington, D.C. 20005. Second-class postage (publication No. 484460) paid at Washington, D.C., and at an additional entry. Now combined with **The Scientific Monthly**®. Domestic individual membership and subscription (51 issues): $56. Domestic institutional subscription (51 issues): $93. Foreign postage extra: Canada $24, other (surface mail) $27, air-surface via Amsterdam $65. First class, airmail, school-year, and student rates on request. Single copies $2.50 ($3 by mail); back issues $3 ($3.50 by mail); Biotechnology issue, $5 ($5.50 by mail); classroom rates on request. **Change of address:** allow 6 weeks, giving old and new addresses and seven-digit account number. Authorization to photocopy material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that the base fee of $1 per copy plus $0.10 per page is paid directly to CCC, 21 Congress Street, Salem, Massachusetts 01970. The identification code for *Science* is 0036-8075/83 $1 + .10. **Postmaster:** Send Form 3579 to *Science*, 1515 Massachusetts Avenue, NW, Washington, D.C. 20005. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

COVER

Satellite ocean color image showing the distribution of phytoplankton pigments around the Galápagos Islands during El Niño. This computer-processed image, color-coded according to concentration range, was produced from data collected on 1 February 1983 using the Coastal Zone Color Scanner aboard NASA's Nimbus-7 satellite. Regions of high concentrations (above 1 milligram per cubic meter) are orange; intermediate levels, yellow and green; lowest levels (less than 0.2 milligram per cubic meter), blue. Major islands are black and clouds white. North is at the top; equator lies horizontally just above the center of the image. See page 1069.[G. Feldman, State University of New York, Stony Brook 11794; D. Clark, National Oceanic and Atmospheric Administration, Washington, D.C. 20233; and D. Halpern, National Oceanic and Atmospheric Administration, Seattle, Washingon 98115]

merican Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objects further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, rove the effectiveness of science in the promotion of human welfare, and to increase public understanding and ciation of the importance and promise of the methods of science in human progress.

LETTERS

Models of Carcinogenesis

Nicholas A. Ashford *et al.*, in their response to comments on their article (Letters, 11 May, p. 554), raise several important issues about low-dose extrapolation models for carcinogens. I would like to comment on an additional and critical element of no-threshold models, using the one-hit, no-threshold model as an example.

The one-hit, no-threshold model for low-dose extrapolation of the dose-response relationship for carcinogens predicts a finite probability that a single molecule can evade the body's defenses and produce an event that triggers cancer. A toxicological threshold is a dosage at or below which no adverse response is observed.

This "no-threshold" concept has received widespread publicity in both the popular and scientific literature and has served as a focal point for criticism of the model. Reduction of this argument ad absurdum has resulted in legislation such as the Delaney clause of the Federal Food, Drug, and Cosmetic Act (*1*). This clause requires that any substance used as a food additive and demonstrated to be a carcinogen in either an animal bioassay or human study must be banned from all food products.

It is critical that the one-hit, no-threshold model be placed in the context of the stochastic (probabilistic) relationship in which it was developed. Although it is theoretically possible that a single molecule of a carcinogen could induce cancer, the probability of this occurrence is vanishingly small. The carcinogenic potential of a chemical substance is a function of both potency and dose. According to the one-hit theory, both of these variables directly and proportionally affect the derived probability that a carcinogenic event will occur. Carcinogens vary in potency by approximately 12 orders of magnitude, and hence there is a wide range of carcinogenic probabilities for any specified dosage of different carcinogens.

For example, benzene is a moderately potent, proven human and animal carcinogen. Low-dose extrapolation from occupational studies using the one-hit, no-threshold model suggests that persons drinking water containing 1 part per billion (weight to volume) (1.0 microgram per liter) of benzene throughout their lives might have an added risk of cancer (excess cancer risk) as high as approximately 2×10^{-6} (*2*) (two additional cases of cancer for every million people so exposed).

The probability of cancer from a single molecule of benzene per liter of drinking water is readily calculable by using this model. If one assumes that the average person weighs 70 kilograms and drinks 2 liters of water per day for a lifetime, the excess carcinogenic risk of drinking water contaminated with one molecule of benzene per liter, a lifetime consumption of about 51,000 molecules of benzene, is approximately 10^{-22}. This risk is more than 16 orders of magnitude smaller than the most stringent state or federal regulatory standard for an allowable risk level of 1×10^{-6} (one in a million excess lifetime risk of cancer). Assuming that the present total world population is 5 billion people and that it consumes this "contaminated" water, one would not expect even one additional case of cancer from this contaminated water, since the probability of one excess case of cancer's occurring in the world's population is 5×10^{-13}.

The fact is that both factions in this argument are correct. According to the no-threshold, one-hit model, there is a finite probability that one molecule of a carcinogen could cause cancer; however, the opponents of this theory are also correct in expressing their incredulity at this possibility. For all practical purposes, the probability of this occurring is so slight as to make this skepticism reasonable. The fact that this model allows for the possibility that one molecule of a carcinogen can induce cancer does not invalidate the model. On the contrary, because the model itself predicts that the occurrence of even a single cancer case from a single molecule of a carcinogen is highly unlikely, the model is able to reflect the known pharmacokinetics and enzymology at extremely low doses rather than totally dismissing this carcinogenic potential by assuming an absolute threshold.

NORMAN GRAVITZ
Epidemiological Study Section, California Department of Health Services, 2151 Berkeley Way, Berkeley 94704

References and Notes

1. Public Law 85-929, 72 Stat. 1784 (1958).
2. Environmental Protection Agency value for the low-dose slope of 0.052 (milligrams per kilogram per day)$^{-1}$ based on R. A. Rinsky, R. J. Young, and A. B. Smith ["Leukemia in benzene workers," *Am. J. Ind. Med.* **2**, 217 (1981)] and provided in *Health Assessment Document for Acrylonitrile* [(EPA-600/8-82-007, Environmental Protection Agency, Washington, D.C., 1983), p. 13-165].

30 November 1984, Volume 226, Number 4678 **SCIENCE**

Environmental Risk Management

Although the Environmental Protection Agency has compiled a reasonably good record during its 13-year history, its prestige has never matched its accomplishments. When the agency began its operations, municipal sewers were discharging large quantities of untreated waste into streams. Industrial stacks were emitting millions of tons of particulates. Automobiles were discharging ten times as much pollution per mile of travel as they do now. Today the water in Lake Erie is said to be drinkable, and fish have returned to formerly polluted rivers.

However, these accomplishments are ignored and EPA finds itself in a virtually untenable position as it seeks to deal with concerns about toxic chemicals. In part, the problem stems from lack of information concerning the toxicities of the over 65,000 different industrial chemicals listed as having been in commercial production since 1945. Contributing heavily to EPA management problems is the fact that it operates under eight different federal environmental statutes, each dealing with a different aspect of environmental protection and each carried out in different branches of EPA. Some of the eight statutes require or allow EPA to base its regulatory decision directly on risk reduction regardless of cost. Other regulatory decisions, such as control of toxic pollutants in the Clean Water Act Effluent Guidelines Regulations, are to be based on available technology and cost instead of risk reduction. As a result of such differing mandates, program integration has been a continuing problem for the leadership of EPA. Failure to coordinate has led to duplicative research and uncoordinated regulation of the same industry or same substance by different programs.

The combination of lack of knowledge of the toxicities of chemicals and internal inconsistencies in EPA has left the agency vulnerable when confronted with unfounded claims of great hazards to the public. The media are seemingly uncritical in their treatment of so-called deadly chemicals. In recent scares about dioxin they have roused sufficient public anxiety to force the agency to give a minor matter top attention at the expense of more important risks to the public.

The EPA has been moving toward a more surefooted and internally consistent approach that is set forth in a report on risk assessment and risk management.* Emphasis is being placed on identifying and reducing major risks. This is to be accomplished by a two-step process—risk assessment followed by risk management. Risk assessment takes into account such evidence as is available about toxicity. More important, it factors in the degree and extent of exposure of the populace to the agent. When such an analysis was performed with respect to a proposed regulation of benzene emissions from maleic anhydride and ethylbenzene plants and benzene storage plants, the regulation was subsequently withdrawn. It was found that the total expected incidence of leukemia arising from such emissions was one case in 13 years. In the same period more than 4 million deaths would occur from cigarette-induced cancer.

Risk assessment of toxic chemicals will remain controversial. Most studies are performed on animals whose sensitivity is well known to differ in unpredictable ways from that of humans. The assumption of a no-threshold effect for carcinogens is also unproved. However, it is the intention at EPA to arrive at internal consistency in risk assessment and then to make public the basis for its assessment. Risk management will then occur with procedures and decisions dictated by the relevant federal statutes.

The EPA is to be commended for arriving at a sensible policy for identifying and managing environmental risks. When the public understands what is being done, the agency should encounter less capricious buffeting and should be more free to formulate an appropriate set of priorities to its tasks of improving the environment.—PHILIP H. ABELSON

*Environmental Protection Agency, *Risk Assessment and Risk Management: Framework for Decisionmaking* (Washington, D.C., in press).

The Division of Cancer Etiology

National Cancer Institute

Announces To The Scientific Community The Availability Of The Following Resources/Services For Cancer Related Research As Noted Below:

Biological Resources

Avian Myeloblastosis Virus Reverse Transcriptase—2,000 Unit Minimum Order

Contact: Life Sciences, Inc.
2900 72nd Street North
St. Petersburg, FL 33710
(813) 346-9371
Citing Contract #N01-CP-11013

Cost: $0.07/Unit Plus Shipping

Cell Culture Identification Service, Using Isozyme Analysis, Immunofluorescence and Karyotypic Analysis (Chromosome Banding)

Contact: Dr. Ward Peterson
Children's Hospital of Michigan
3901 Beaubien Boulevard
Detroit, MI 48201
(313) 494-5705
Citing Contract # N01-CP-21017

Cost: $200.00/Analysis

Goat Antisera against: Avian, Bovine, Feline, Murine, and Primate Intact Viruses and Viral Proteins; Antibodies to Immunoglobulins for a number of species. Preimmune Sera available for some Virus Antisera

Contact: Coordinator for Research Resources
Biological Carcinogenesis Branch, DCE, NCI, NIH
Landow Bldg., Room 9A22
Bethesda, MD 20205
(301) 496-1951

Cost: $10.00/ml Plus Shipping (Pre-Immune Sera—$5.00/ml)

Viruses: Avian, Feline, Murine, and Primate Viruses Prepared in Tissue Culture

Contact: Coordinator for Research Resources
Biological Carcinogenesis Branch, DCE, NCI, NIH
Landow Bldg., Room 9A22
Bethesda, MD 20205
(301) 496-1951

Cost: Inquire

Baboon Sera Collected from Animals in Sukhumi, USSR with High and Low Incidence of Malignant Lymphoma

Contact: Coordinator for Research Resources
Biological Carcinogenesis Branch, DCE, NCI, NIH
Landow Bldg., Room 9A22
Bethesda, MD 20205
(301) 496-1951

Cost: Shipping Charges Only

Sera from Primates which were housed in the U.S. and Inoculated with Material from the Sukhumi Baboons

Contact: Coordinator for Research Resources
Biological Carcinogenesis Branch, DCE, NCI, NIH
Landow Bldg., Room 9A22
Bethesda, MD 20205
(301) 496-1951

Cost: Shipping Charges Only

Human Tissues: Carcinomas, Sarcomas, Melanomas, Lymphomas, Leukemias, Benign Tumors and other Non-Malignant Disorders

Human Sera from donors with: Carcinomas, Sarcomas, Melanomas, Lymphomas, Leukemias, Benign Tumors, Normal Individuals, Family Members of Leukemics, Hematological Diseases, and other Non-Malignant Disorders

Contact: Coordinator for Research Resources
Biological Carcinogenesis Branch, DCE, NCI, NIH
Landow Bldg., Room 9A22
Bethesda, MD 20205
(301) 496-1951

Cost: Shipping Charges Only

Cotton-Top Marmosets *(S. oedipus)* for Use as Models for Carcinogenesis—Holding, Inoculation, Observation, and Pathology Services are Available

Contact: Dr. Neal Clapp
Marmoset Research Program
Oak Ridge Associated Universities
P.O. Box 117
Oak Ridge, TN 37831
(615) 576-4103
Citing Contract #N01-CP-21004

Cost: $10.00 per diem (or higher for procedures involving additional care, etc.) $10.00 per blood sample

Chemical Resources

Chemical Carcinogen Reference Standard Repository: Reference Quantities of nearly 700 compounds are available. Included are numerous representatives of the following classes: polynuclear aromatic hydrocarbons, PAH metabolites, radiolabeled PAH metabolities, nitrogen heterocycles, nitrosamines/nitrosamides, aromatic amines, aromatic amine metabolites, radiolabeled retinoids, azo/azoxy aromatics, inorganics, nitroaromatics, pesticides, pharmaceuticals, natural products, dyes, dioxins, chlorinated aliphatics and miscellaneous groups. Data sheets provided with the compounds, include chemical and physical properties, analytical data, hazards, storage, and handling information. Catalog available upon request.

Contact: Coordinator for Chemical Research Resources
Chemical and Physical Carcinogenesis Branch, DCE, NCI
Landow Bldg/Rm 9B01
Bethesda, MD 20205
(301) 496-5471

Cost: Subject to chemical class code and quantity (see catalog)

Epidemiology Resources

The Immunodeficiency—Cancer Registry (ICR) is a unique registry of cancer cases that occur in patients with naturally-occurring immunodeficiencies. Case material collected by the ICR comes from case reports appearing in scientific literature and voluntary reporting by physicians. Criteria for inclusion in the registry are clinical or laboratory evidence of a primary immunodeficiency syndrome prior to the onset of malignancy. Data contained in the ICR are available to the extramural research community for the planning, design, and conduct of research efforts. Limited assistance is available to investigators interested in utilizing the registry.

Contact: Dr. Alexandra H. Filipovich
Immunodeficiency—Cancer Registry
Box 610 Mayo
University of Minnesota
Minneapolis, MN 55455
(612) 376-2174
Citing Contract #N01-CP3-1011

The Tumor Virus Epidemiology Repository (TVER), contains sera and other biological samples from more than 13,000 patients and controls obtained in 12 different countries. The TVER was established primarily to support collaborative research on the role of Epstein-Barr virus (EBV) in Burkitt's lymphoma, nasopharyngeal carcinoma, and related diseases. Part of the collection includes sera that were obtained from nonhuman primates inoculated with EBV.

The TVER is able to adjust its collection to facilitate the development of new collaborative studies. In addition, some samples are available for reagents and independent research. The most extensive collections are serum samples from patients with Burkitt's lymphoma (sera from more than 1000 patients).

Contact: Dr. Paul H. Levine
Clinical Epidemiology Branch, DCE, NCI, NIH
Landow Building, Room 8C41
Bethesda, MD 20205
(301) 496-5067

Cost: Free to Collaborating Investigators; Others—Shipping Charges Only