THE CANCER LETTER

Vol. 21 No. 39
Oct. 13, 1995

Price $255 Per Year US
$280 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

NCI's New Divisional Structure In Place, Next Step Is Review Of Labs, Branches

Completing the first phase of a reorganization Richard Klausner outlined at the time of his appointment as NCI Director, the Institute last week put in place a new divisional structure.

*As of Oct. 1, NCI's intramural and extramural programs were placed into separate divisions, following a recommendation of a committee of the National Cancer Advisory Board (**The Cancer Letter**, July 7, 14 & 21).*

(Continued to page 2)

In Brief

Three Scientists Share Nobel Prize For Work In Genetics; Clinton Forms Bioethics Panel

NIH GRANTEES Eric Wieschaus, of Princeton Univ., **Edward Lewis,** of California Institute of Technology, and **Christiane Nusslein-Volhard**, of the Max Planck Institute in Germany, received the Nobel Prize for physiology or medicine for their research on genes that control embryonic development. Their work, based on the fruit fly, Drosphila, has been supported by the National Institute of Child Health and Human Development and the National Institute of General Medical Sciences. . . . **PRESIDENT CLINTON** last week called for a review of measures to protect human research subjects and established a National Bioethics Advisory Commission. The executive order calls for each department and agency that conducts, supports, or regulates research involving human subjects to review the "protections of the rights and welfare" of human research subjects under existing policies and procedures. The commission also should address "issues in the management and use of genetic information, including but not limited to, human gene patenting," according to the executive order. . . . **UNIV. OF MICHIGAN** Comprehensive Cancer Center has appointed four new faculty members to leadership positions. **Eric Fearon**, formerly an assistant professor at Yale Univ., was named associate director for basic research and Maisel Professor of Oncology. **Victor Strecher**, formerly associate professor of health behavior at Univ. of North Carolina, was appointed to the new position of associate director for cancer prevention and control. **Vicki Baker**, associate professor of obstetrics and gynecology at Univ. of Texas-Houston Health Science Center, was named director of gynecologic oncology, and the George W. Morley Professor of Obstetrics and Gynecology and chief of the Div. of Gynecologic Oncology. **KyungMann Kim**, associate professor at Harvard School of Public Health, was appointed associate professor of biostatistics and director of the biostatistics core at the cancer center.

NCI Committees To Search For Permanent Div. Directors

(Continued from page 1)

At the same time, the Institute's former five divisions were split into seven, with several of the divisions being renamed to reflect their new areas of emphasis (**The Cancer Letter**, Sept. 15).

Moving to the next phase, NCI officials are proceeding to the reorganization of laboratories and branches within the new divisions.

A list of the divisions, as well as key addresses and telephone numbers appears on page 3. **The Cancer Letter** intends to publish an NCI directory after the reorganization is completed.

Though the new organizational structure is now in place, the advisory boards remain to be appointed, NCI officials said.

Last week, the absence of new advisory boards caused a logistical problem for the newly formed Div. of Cancer Epidemiology and Genetics, which encompasses several the functions of the former Div. of Cancer Etiology. To approve concepts for grant and contract programs involving epidemiology, the division sought approval from the Board of Scientific Counselors of the former DCE. (See story, page 5).

Adding to the difficulty, Congress has not completed the appropriations process for the Dept. of Health and Human Services, which includes NCI. Congress passed a continuing resolution that provides agencies with budgets equal to 95% of their fiscal 1995 appropriations. The resolution expires Nov. 15.

The DCE board's acting chairman, Nancy Mueller, professor of epidemiology at the Harvard School of Public Health, noted the irony of the transitional nature of NCI last week. "I am the acting chair of a Board of Scientific Counselors that is meeting for the last time for a division that ceased to exist a few days ago, and on our agenda today is a discussion of a budget that has not been passed," said Mueller introducing herself to the board.

Jerry Rice, acting DCE director until last week, said the Institute has been relatively stable over the past few months.

"When I accepted the position of acting director [in the fall of 1994], the period was a tumultuous one," Rice said to the board. "There were persistent rumors that the entire DCE would be loaded on trucks and moved to North Carolina to populate new buildings at the National Institute of Environmental Health Sciences."

In addition, a long hiring freeze made it impossible to fill key positions, and the division's first candidate for tenure under the new NIH tenure process had been rejected, Rice said. Ultimately, 23 young investigators from DCE were grandfathered into the tenure program, and Rice made several appointments to fill vacant branch chief positions.

Under the new structure, the NCI intramural program will be organized into two divisions, the Div. of Basic Sciences and the Div. of Clinical Sciences. DBC is headed by George Vande Woude and DCS is headed by Philip Pizzo.

In other changes:

•The former Div. of Cancer Etiology becomes the Div. of Cancer Epidemiology and Genetics, giving division status to the epidemiology and biostatistics program. DCE's laboratories move to the basic sciences division. Acting Director: Joseph Fraumeni.

•The former Div. of Cancer Biology, Diagnosis and Centers sheds its intramural laboratories and the diagnosis and cancer centers programs to become the predominantly extramural Div. of Cancer Biology. Acting Director: Faye Austin.

•The former Div. of Cancer Treatment loses its intramural clinical programs to the clinical sciences division, but gains the diagnosis and cancer centers program. The division's new name is the Div. of Cancer Treatment, Diagnosis and Centers. Acting Director: Robert Wittes.

•Two divisions remain essentially as they were: the Div. of Cancer Prevention and Control, which loses its two wet labs to the intramural divisions, and the Div. of Extramural Activities, which continues to oversee grants and contracts management.

DCPC and DEA are the only two divisions led by directors who held those positions prior to

THE CANCER LETTER

Editors: **Kirsten Boyd Goldberg**
Paul Goldberg

Founder & Contributing Editor: **Jerry D. Boyd**

P.O. Box 15189, Washington, D.C. 20003
Tel. (202) 543-7665 Fax: (202) 543-6879
E-Mail: 73322.2044@compuserve.com

Subscription $255 per year US, $280 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter.

Klausner's appointment. DCPC is headed by Peter Greenwald and DEA is headed by Marvin Kalt.

Though Klausner has named acting directors for five of the divisions, committees are being formed to conduct national searches for permanent directors.

"There is the feeling that NIH in the past has appointed too many people from within, and we haven't reached out on a national level to find the best people," NCI Deputy Director Alan Rabson said to the DCE board last week. "Even so, the acting directors are really moving ahead; they are not stationary."

Now that the divisional structure is in place, the next step is to review all the components within the divisions, particularly in the Div. of Basic Sciences, *which has 33 laboratories*, Rabson said to the DCE board.

"We want to review all [the laboratories], conduct a serious review and decide which ones to [merge]," Rabson said.

New NCI Divisional Structure And Phone Numbers Listed

The revised NCI divisional structure with a partial listing of laboratories and branches, phone numbers and addresses follows. All mailing addresses are Bethesda, MD 20892-[MSC number], except as noted.

Office of Director

Director, Dr. Richard Klausner
31 Center Drive Room 11A48 MSC 2590
Bethesda, MD 20892-2590
301-496-5615; fax: 301-402-0038
e-mail: Klausner@helix.nih.gov

Deputy Director, Dr. Alan Rabson
31 Center Drive Room 11A48 MSC 2590
301-496-1927; fax: 301-402-0338

Legislative Liaison, Dorothy Tisevich
31 Center Drive Room 11A21 MSC 2590
301-496-5217; fax: 301-402-1225

Associate Director for Strategic Planning, Dr. Edward Sondik
31 Center Drive, Room 10A49 MSC 2580
301-496-9569; fax: 301-496-9931
e-mail: sondikE@od.nci.nih.gov

Office of Extramural Management
Associate Director, Philip D. Amoruso
31 Center Drive Rm 11A48 MSC 2590
301-496-5737; fax: 301-496-2471

Office of Intramural Management
Associate Director, MaryAnn Guerra
31 Center Drive Room 11A29 MSC 2590
301-435-2455; fax: 301-435-2396
e-mail: mge16@nih.gov

Office of Cancer Communications
Associate Director, J. Paul Van Nevel
31 Center Drive Room 10A31 MSC 2580
301-496-6631; fax: 301-402-4945

International Cancer Information Center
Associate Director, Susan Hubbard
Bldg 82 Rm 102
301-496-9096; fax: 301-480-8105
e-mail: su@icic.nci.nih.gov

Office of International Affairs
Associate Director, Dr. Frederico Welsch
6130 Executive Blvd. Room 100 MSC 7301
301-496-4761; fax: 496-3954
e-mail: nc6@cu.nih.gov

Office of Program Operations & Planning
Associate Director, Iris Schneider
31 Center Drive Room11A48 MSC 2590
301-496-5534; fax: 301-402-0338
e-mail: schneidi@od.nci.nih.gov

Office of Laboratory Animal Science
Associate Director, Dr. Patricia Brown
31 Center Drive Room 4B59
301-496-866

Office of Technology Development
Associate Director, Dr. Thomas Mays
31 Center Drive Room 4A51
301-496-0477; fax: 301-402-2117
e-mail: mayst@otd.nci.nih.gov

Div. of Basic Sciences

Acting Director, Dr. George Vande Woude
31 Center Drive Room 3A11
301-496-4345; fax 301-496-0775
NCI-FCRDC PO Box B Bldg 469 Room 246
Frederick, MD 29702
301-846-1584 or 5210; fax 301-846-5038
e-mail: woude@ncifcrf.gov

Experimental Immunology Branch
Laboratory of Immunobiology
Varmus Laboratory
Laboratory of Tumor Immunology and Biology

Laboratory of Biochemistry
Laboratory of Cell Biology
Laboratory of Cellular Oncology
Laboratory of Genetics
Laboratory of Molecular Biology
Laboratory of Experimental Pathology
Laboratory of Molecular Oncology
Laboratory of Molecular Virology
Laboratory of Cellular and Molecular Biology
Laboratory of Viral Carcinogenesis
Laboratory of Tumor Virus Biology
Laboratory of Tumor Cell Biology
Laboratory of Biology
Laboratory of Molecular Carcinogenesis
Laboratory of Chemoprevention
Lab. of Cellular Carcinogenesis & Tumor Promotion
Laboratory of Experimental Carcinogenesis
Laboratory of Human Carcinogenesis
Laboratory of Comparative Carcinogenesis
Laboratory of Experimental Immunology
Laboratory of Biochemical Physiology
Laboratory of Medicinal Chemistry
Laboratory of Nutritional & Molecular Regulation
Laboratory of Molecular Immunoregulation
Laboratory of Leukocyte Biology
Laboratory of Immune Cell Biology
Laboratory of Molecular Pharmacology
Laboratory of Mathematical Biology
Laboratory of Biological Chemistry

Div. of Clinical Sciences

Acting Director, Dr. Philip Pizzo
31 Center Drive Room 3A11
301-496-3251; fax: 301-496-0775
e-mail: pizzop@pbmac.nci.nih.gov
Dermatology Branch
Metabolism Branch
Laboratory of Pathology
Surgery Branch
Medicine Branch
NCI-Navy Medical Oncology Branch
Pediatric Branch
Radiation Oncology Branch
Radiation Biology Branch
Clinical Pharmacology Branch
Clinical Research Branch
Biomarkers and Prevention Research Branch

Div. of Cancer Epidemiology and Genetics

Acting Director, Dr. Joseph Fraumeni
6130 Executive Blvd Room 543 MSC 7399
Rockville, MD 20852-7399
301-496-1611; fax: 301-402-3256
e-mail: fraumenj@epndce.nci.dce.gov

Div. of Cancer Prevention & Control

Director, Dr. Peter Greenwald
31 Center Drive Room 10A52 MSC 2580
301-496-6616; fax: 301-496-9931
Deputy Director, Dr. Edward Sondik
31 Center Drive, Room 10A49 MSC 2580
301-496-9569; fax: 301-496-9931
e-mail: sondikE@od.nci.nih.gov

Div. of Cancer Treatment, Diagnosis & Centers

Acting Director, Dr. Robert Wittes
31 Center Drive Room 3A44 MSC 2440
301-496-4291; fax: 301-496-0826
e-mail: wittes@nih.gov
Cancer Diagnosis Branch
Biological Resources Branch
Radiation Research Program
- Radiotherapy Development Branch
- Diagnostic Imaging Branch

Cancer Therapy Evaluation Program
- Investigational Drug Branch
- Biometrics Research Branch
- Clinical Investigations Branch
- Clinical Trials Monitoring Branch
- Pharmaceutical Management Branch
- Regulatory Affairs Branch

Developmental Therapeutics Program
- Information Technology Branch
- Biological Testing Branch
- Grants and Contracts Operations Branch
- Toxicology and Pharmacology Branch
- Lab. of Drug Discovery & Research Development
- Laboratory of Pharmaceutical Chemistry
- Antiviral Evaluations Branch
- Natural Products Branch
- Drug Synthesis and Chemistry Branch
- Pharmaceutical Resources Branch

Centers, Training and Resources Program
- Cancer Centers Branch
- Organ Systems Coordinating Branch
- Cancer Training Branch
- Research Facilities Branch

Div. of Cancer Biology

Acting Director, Dr. Faye Austin
6130 Executive Blvd Room 500
Rockville, MD 20892
301-496-8636; fax: 301-496-8656

Div. of Extramural Activities

Director, Dr. Marvin Kalt
6130 Executive Blvd Room 600
Rockville, MD 20892
301-496-5147

DCE Board Sets Aside $2 Mil. For Radiation Grants Program

Advisors to the former NCI Div. of Cancer Etiology agreed to set aside $2 million in fiscal 1996 to fund grants in the study of genomic instability of mammalian cells exposed to radiation.

The new grants program was proposed by participants in a workshop held earlier this year by NCI's Radiation Effects Branch and the Life Sciences Division of the National Aeronautics and Space Administration.

The DCE Board of Scientific Counselors, at its final meeting last week, approved the concept for a Request for Applications for the grants program.

The advisory board also approved a concept for a new contract for the immunoepidemiologic study of low-grade squamous intraepithelial lesions of the cervix. This would be an add-on study to the ASCUS trial conducted by the NCI Div. of Cancer Prevention and Control.

In addition, the board approved the recompetition of two support contracts and several noncompetitive contracts and interagency agreements.

The excerpted concept statements follow. For further information, contact the program directors or project officers listed. When the RFAs and RFPs are issued, they will appear in **The Cancer Letter**.

Mechanisms of Transmissible Genomic Instability from the Exposure of Mammalian Cells to Ionizing Radiation. Concept for an RFA, proposed first year funding $2 million ($1 million from NCI, $1 million from NASA). Program directors: Richard Pelroy, NCI Chemical and Physical Carcinogenesis Program, Radiation Effects Branch; Walter Schimmerling, NASA.

This proposed RFA will support the investigation of mechanistic studies of the molecular basis of high-LET-induced TGI in undifferentiated primary cells that are representative of different cell types and tissues (e.g., bone marrow, breast) from humans or animal models. High-energy protons, HZE and alpha particles and low-energy neutrons will be emphasized as the main relevant sources of high-LET radiation. The focus is on two general research areas: (1) the analysis of the DNA lesions and cellular processes that perpetuate high-LET-induced TGI (i.e., primarily from exposures to HZE particles or high-energy protons) and (2) the relationships of such high-LET-induced TGI to neoplastic transformation among progeny of irradiated cells.

1. Perpetuating Events: This area addresses both the nature of unstable DNA sequences that undergo alteration during expression of TGI and the possible mechanisms that could account for both chromosomal and/or genetic instability during expression of the TGI phenotype over many generations. It can include, but is not limited to:

•The role of regulation of cell growth in high-LET-damaged cells on the subsequent expression of TGI,

•The identification of DNA-sequences that become unstable during expression of TGI, their mechanisms of formation, and the analysis of the mutational changes that they undergo,

•Studies to determine if there is a cytogenetic mechanism to account for both the chromosomal and the genetic instability observed in cells expressing TGI,

•The role of recombination on the expression of the TGI phenotype.

2. Relationship of High-LET-Induced TGI to Neoplastic Transformation: This objective addresses use of both in vitro and in vivo studies in animal models to determine if the expression of high-LET-induced TGI by undifferentiated, preneoplastic stem cells predisposes them to neoplastic transformation. It could include, but is not limited to:

•Parallel in vitro and in vivo studies with the same preneoplastic cell to determine if there is a concordance of events during expression of TGI in vitro and in vivo and possible relationships of such events observed during the development of neoplastic transformation.

•The timing of the expression of a "mutator" phenotype among the progeny of irradiated cells that are progressing to cancer and the relationship of this phenotype to loss of growth and radiation checkpoint control during expression of TGI.

Prospective Immunoepidemiologic Study of Low-Grade Squamous Intraepithelial Lesions of the Cervix (Low-Grade SIL). Concept for a new contract (RFP), proposed total $1.159 million over four years. Project Officers: Allan Hildesheim, Howard Strickler, Mark Schiffman, Epidemiology and Biostatistics Program.

It is now established through experimental and epidemiologic evidence that human papillomavirus (HPV) infection causes most cases of cervical carcinoma and its precursors, which are divided into low-grade and high-grade squamous intraepithelial lesions (SIL).

To date, studies that have investigated the immune determinants of progression of low-grade SIL to high-grade SIL have largely been cross-sectional and small. However, there is now an opportunity to investigate this issue in a large, well-characterized prospective cohort. We propose to incorporate an add-on study to a large clinical trial of the management of low-grade SIL currently being planned by the Div. of Cancer Prevention and Control. This $17 million, six-year trial of 7200 women, just beginning formal protocol development, is designed to evaluate proper triage of women with low-grade SIL and the even more common equivocal diagnosis of ASCUS (atypical squamous cells of undetermined

significance, i.e., equivocal SIL). As part of this trial, 3600 women with low-grade SIL diagnosed in the community will be enrolled at one of four clinical centers. One-third of the participants (1200 cases of low-grade SIL) will be randomized into the "expectant management" arm of the trial (as opposed to the "HPV typing triage" arm or the "immediate colposcopy" arm). Follow-up of women in the expectant management protocol is planned to include semi-annual cytology and cervicography. Cervicography is a magnified visual screening of the cervix following acetic acid staining to highlight lesions. Upon careful review of enrollment findings, about 10% of these women are expected to have high-grade lesions (high-grade SIL) confirmed by colposcopically-directed biopsy. All other women will be actively followed and retested every six months for three years. This will provide the ideal population in which to investigate immune factors related to progression. Already incorporated into each clinic visit in the trial is the collection of cervical cells for HPV DNA testing and a risk factor questionnaire to elicit information on potential exogenous co-factors.

The proposed new procurement would add expanded collection of blood and cervical specimens to the project for a large cross-sectional and prospective investigation of immune factors related to disease progression, persistence, and regression.

Objectives: Promising cellular and humoral immune parameters will be investigated to evaluate the immune predictors of progression, persistence, and regression of low-grade SIL. Initially, women will be evaluated in a cross-sectional fashion, followed by a prospective assessment of which immune biomarkers predict disease outcome. Specific emphasis will be placed on evaluating the role of a Thl type of immune response, immunoglobulin production (by class and subclass), and HLA haplotypes as determinants of clinical outcome. Host responses will be correlated with corresponding viral state (e.g., examining whether a Thl response leads to a decrease in HPV viral load concurrent with regression of the low-grade SIL), and will be examined in the context of other cervical cancer risk factors.

Methods: Endpoints in this study include persistent low-grade SIL, regression of existing low-grade lesions, and progression to high-grade SIL. High-grade SIL is the "surrogate" endpoint for invasive carcinoma in this study, given that follow-up to invasion itself would be unethical and is not expected to occur.

The 1200 women with low-grade SIL randomized to expectant management in the large DCPC-sponsored clinical trial will be approached, with separate informed consent, to participate in this add-on project. The larger trial will begin protocol development following contract awards in October 1995. Starting in the summer of 1996, women will be recruited from the four clinical centers selected to participate in the larger trial. These women are scheduled to be followed without colposcopic referral, biopsy, or treatment unless they have an enrollment review or follow-up Pap smear or cervigram suggesting high-grade SIL. Collection of specimens will be coordinated with clinic visits already planned as part of the DCPC trial; no additional clinic visits will be required. We will collect blood and cervicovaginal lavage specimens initially from a maximum of 1200 women (if all accept the additional protocol because of its minimal demands).

Enrollment Phase: We propose to add the collection of more peripheral blood (to harvest viable lymphocytes) and a cervicovaginal lavage (for cervical secretions) at the time of the initial enrollment visit. Blood will be shipped fresh to the study laboratory, where T-cell function tests will be performed, including tests that measure T-cell responses to specific HPV antigens. The remainder of the blood will be separated by centrifugation, and plasma and cryopreserved lymphocytes will be prepared and frozen for future testing. Cervicovaginal lavages will also be frozen and used for future testing of mucosal antibodies. We propose to collect fresh biopsy material from those subjects referred from the enrollment visit to colposcopy. This material will permit the investigation of tissue infiltrating lymphocytes.

With regard to study size, all 1200 women referred for low-grade SIL and randomized into the expectant arm will be included in the cross-sectional phase. As a result of the trial's expert evaluation of the referral and enrollment cytology, we estimate that 10% (N=120) of subjects will be upgraded to high-grade SIL after being sent to colposcopy/biopsy based on suspicious cervicographic or cytologic findings. About 70% of subjects (N=840) referred from the community for presumed low-grade SIL will be confirmed as truly having low-grade SIL, 15% of whom will be confirmed as having low-grade SIL only after being sent to colposcopy/biopsy because of findings during cervicography or cytology review. Additionally, we expect that 20% (N=240) of the women will be downgraded to normal. The clarified diagnoses provided by the expert review will form the basis of our prevalent case-control study, in which immune response and function will be evaluated cross-sectionally among normal women and those diagnosed with low-grade SIL and high-grade SIL.

Follow-up Phase: Biological samples will be available for all 1200 women with possible low-grade SIL diagnosis at enrollment into the study. This will permit us to correlate baseline measurements of immune status and function with disease outcome over the three year course of follow-up. In addition, we plan to perform time-dependent analyses in which women who regress at each time interval are compared to those who persist or progress during the same time period. Specifically, we propose to collect repeated, follow-up biological

samples from a group of 200 randomly-selected study participants. In keeping with the follow-up schedule planned for the larger clinical trial, this group of 200 women will be followed every six months for an average of three years. The repeated measurements will permit us to examine the immune responses that occur at or about the time of clearance of lesions and the underlying HPV infections. We estimate that about 40% of women will regress cytologically in the first year of follow-up alone. In addition, we propose to enroll for repeat measurement all women who progress to high-grade SIL during the course of follow-up and are sent for colposcopic evaluation as part of trial procedures (no carcinomas are expected). It is anticipated that 3-5% of the 840 subjects with a confirmed diagnosis of low-grade SIL (n= 25-42) will progress during follow-up.

Both time-dependent and cumulative analyses are planned for the follow-up phase of the study.

Type of Awards: Three types of awards will be made for this procurement. DCPC contracts awarded competitively to four clinical centers selected to participate in the trial will be supplemented to permit the additional collection and shipment of biological specimens. We also propose to supplement the contract which will be made shortly by DCPC to the offeror selected to coordinate the trial efforts. This coordinating center will assist in the development of study protocols and forms, will coordinate efforts across clinical sites and laboratories, and will be responsible for receiving, editing, and computerizing data collected as part of the project. Finally, contracts will be made competitively to commercial laboratories for the processing of biological specimens collected as part of this study as well as for the planned assays, particularly the testing of fresh samples for T-cell responses to recall antigens.

Distribution of Costs: The above concept includes funding for the assays already planned, in addition to the field costs (about $211,000). By far the most expensive assays are the tests of T-cell responses to recall antigens, which involve viable lymphocytes. We have budgeted about $240 per specimen ($576,000 for 2400 assays over the course of the study) for this purpose. HLA testing among the 200 prospectively followed patients and 25 cases expected to progress was budgeted at about $190 per specimen ($42,750). Serologic assays were budgeted at $60 per subject ($144,000) as a whole, and include HPV antibodies, neopterin and sIL-2r.

Biological Specimen Repository for Patients at High Risk for Cancer. Recompetition of a contract held by Biological Research Faculty and Facility, total $1.925 million over five years. Project officers: Margaret Tucker, Jeffery Struewing, Epidemiology and Biostatistics Program.

Laboratory studies of persons at high risk for cancer provide opportunities to evaluate the role of host susceptibility and host-environmental interactions in cancer etiology. The Family Studies Group of the Epidemiology and Biostatistics Program (EBP) has pioneered this approach over a 20-year period. Study subjects include: (1) patients with genetic disorders that enhance cancer risk, (2) members of families prone to the same or diverse malignancies, (3) patients with non-neoplastic conditions at high risk of cancer, and (4) those with environmental exposures that may increase cancer risk. This repository is our major cell propagation resource and contains over 3,000 skin fibroblast, epithelioid, lymphoblastoid, and tumor cell lines contributed by members of the EBP, outside collaborators, and other cell banks.

Objectives: To establish fibroblast, epithelioid, tumor, and lymphoblast cell lines; to propagate these cell lines to bulk as requested; to maintain the repository using the most current laboratory techniques for ensuring the highest viability and cell yield from the cultures; and to distribute cell lines to laboratory scientists as requested.
Methods:

1. Transport of specimens: The Contractor will arrange for routine pick-up of specimens at a time and place designated by the NCI Project Officer. Emergency service must be available 24 hours per day, seven days per week for pick-up at area transportation centers, hospitals, private physician offices, or private homes. Pick-up activities must be initiated within one hour of being notified by the Project Officer. Specimens will be delivered to the laboratory within 2-3 hours of pick-up. For this reason, the Contractor must be within one hour's distance from Bethesda. Media for transport of specimens to the lab will be provided by the Contractor. Coded specimens will be sent to collaborating investigators only upon receipt of a written request from the Project Officer.

2. Culture of cells: The Contractor must demonstrate at least two years experience in the successful establishment of fibroblast and lymphoblast cell lines. The Contractor must also demonstrate success with the culture of established tumor cell lines. The tissue culture techniques must be specified in detail, and data must be provided which document the laboratory's current rate of success in establishing cell lines, cell yield, and cell viability. Cultures will be routinely screened for contamination by mycoplasma, bacteria and fungi. Outside cultures will be screened to ensure that the cells are of human origin. Normal fibroblast and lymphoblast cell lines will be established in laboratories where no animal or tumor tissue culture is being performed. Tumor cell lines will be handled in laboratories where no animal cell culture is performed.

3. Storage of cell lines: All cell lines will be stored under optimum conditions in liquid nitrogen freezers. Specimens at any passage will be stored in a least two separate freezers. Freezers must have a constant central source of liquid nitrogen with emergency back-up.

Freezers must have automatic filling mechanisms and 24-hour central sound alarm systems, with active surveillance 24 hours per day, year round, with explicit directions on the steps to take in case of emergency. Each freezer will be checked daily by technical personnel. Specimens should be frozen in containers impervious to entry of atmospheric CO2, such as silicon-sealed "nunc" type tubes so that they can be shipped on dry ice.

4. Inventory of records: The laboratory will keep clear documentation of all manipulations on all cell lines and carefully document passage, "crisis events", growth characteristics, and types of contamination screening performed on each cell line. The exact freezer location will be known for each cell line and passage and will be kept in a master log which is easy to understand. Information will be supplied routinely to the NCI Project Officer on forms designed and supplied by NCI in conjunction with laboratory personnel for computer data entry. These records will include subject ID, specimen ID, growth status, contamination status, number of vials, exact location of vials, passage level, and specimen type.

5. Computer specimen tracking: NCI will provide the computer support for record keeping in the form of our coordinated repository tracking system. The Contractor will enter the tracking information, verify the accuracy of these data, and perform a yearly inventory to verify current locations and numbers of vials.

Interdisciplinary Studies in Occupational Cancer. Recompetition of a contract held by Battelle/Survey Research Associates Inc., total $9.5 million over five years. Project officer: Aaron Blair, Occupational Studies Section.

This concept is a continuation of activities to provide epidemiologic support for the Occupational Studies Section. In the past, it has provided approximately 70% of the contract budget for the Occupational Studies Section. The research effort by the Occupational Studies Section rests on state-of-the-art, interdisciplinary investigations that include epidemiology, industrial hygiene, and laboratory science components. The combination of these three disciplines creates a powerful approach that allows pioneering investigations into the causes of cancer.

The contract for the occupational studies program is used in two ways: 1) to provide personnel and support for data collection and data processing for research projects, and 2) as a mechanism for developing subcontracts with extramural investigators collaborating in our research.

Type of Contract: A new contract will be competed to replace the current one, which expires January 31, 1997. The NCI seeks the assistance of an organization highly experienced in providing technical support in all phases of data collection in occupational health studies including the design of data collection documents; hiring and training of interviewers and abstractors; collecting, keying, editing, updating, and coding data; tracing individuals; monitoring and estimating exposures in the workplace; collecting, processing, transporting, and analyzing biologic tissues and fluids; creating and manipulating data files, and developing and running analytic programs.

The board also approved the following noncompetitive contracts:

—Population-based natural history study of cervical neoplasia in a high-risk region of Latin America. Costa Rican government foundation for medical research, two years, proposed first year award $375,000. Project officer: Mark Schiffman.

—Case-control study of brain tumors. Research Triangle Institute, two years, proposed first year award $475,000. Project officer: Elizabeth Hatch.

—Collaborative Program on Environmental Cancer. Interagency agreement with the Environmental Protection Agency, five years, no request for funding of specific projects. NCI coordinator: Victor Fung.

—Conduct of Research on Occupational Carcinogenesis. Interagency agreement with National Institute for Occupational Safety and Health, five years, no request for funding. NCI coordinator: Victor Fung.

Science Fellowships In Japan Available Through NIH

Through arrangements made with the NIH Fogarty International Center, the Japan Society for the Promotion of Science is offering 30 fellowships for American researchers in the biomedical and behavioral sciences to pursue collaborative research in Japanese universities and other eligible institutions and laboratories.

Funding is available for stays ranging from two weeks to 12 months. The fellowships are intended to enhance American-Japanese collaboration in biomedical and behavioral research by providing flexible opportunities for capable American scientists to work with colleagues in leading Japanese laboratories on substantive projects of mutual interest. Although intended primarily for post-doctoral level researchers, doctoral candidates and senior researchers also may apply. Fellows are expected to be recipients of NIH awards or to be substantially involved in NIH-supported research.

Because recipients must arrive in their host laboratories in Japan by March 31, 1996, interested persons should contact the Fogarty International Center immediately.

Inquiries: Director, Div. of International Relations, Fogarty International Center, ATTN: JSPS Fellowships, Bldg 31 Rm B2C11, 31 Center Dr., MSC 2220, Bethesda, MD 20892-2220, tel: 301/496-4784, fax: 301/480-3414, e-mail: JSPS@NIH.GOV