THE CANCER LETTER

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DCE BOARD APPROVES CONCEPT FOR NEW $850,000 YEAR GRANT PROGRAM TO STUDY VIRUSES IN CERVICAL CANCER

A new grant supported research program to investigate the role of papillomaviruses in the etiology of human cervical cancer, with annual funding estimated at $850,000 a year, was given concept approval by

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In Brief

FY 1985 BUDGET BREAKDOWN: CONTROL GETS $64 MILLION, CONSTRUCTION $6.5; W.VA. $4.5 MAYBE

HERE'S HOW the three major questions left unclear in the appropriations bill Congress approved for NCI probably will be answered: There will be $6.5 million for construction, rather than the $13.5 million asked by the Senate. Up to $4.5 million of that will be available for West Virginia Univ., but whether any or all of it goes to W.Va. depends on peer review. Any that does not go there will be available for other construction grants. Cancer control will get $64 million, up only $1 million over FY 1984. Research training (NRSA) will get $31 million, which will permit paying higher stipends.... **CENTERS ARE** not well thought of at NIH and "are considered the first area to go when budgets are cut," NCI Director Vincent DeVita said at the President's Cancer Panel meeting in Seattle. "Centers are always at risk. This is very distressing to us... OMB has resolutely prevented any additional construction funds and there is no way they will (change) unless Congress and people who feel that we have to rebuild our laboratories get the message across... I am very, very impressed that the amount of money we have put in construction in centers has usually been a quarter to a third of the monies required. When you look at the money that was brought in to build those buildings, it was not money that normally would have come to that institution without the seed money from government. I think these facts are not well received in OMB. We like to pick on OMB. I think we are allowed to pick on OMB, as a matter of fact".... **TWO BRANCH** chief appointments were announced by Div. of Cancer Etiology Director Richard Adamson: David Longfellow, who has been acting chief of the extramural Chemical & Physical Carcinogenesis Branch, has been named permanent chief of that branch. Peter Howley has been named chief of the Laboratory of Tumor Virus Biology.... **DIV. OF CANCER** Prevention & Control is recruiting for another branch chief, the Diet & Cancer Branch. It is a Civil Service position at the GM-15 level, with a salary range from $53,407 to $66,400, with physicians eligible for comparability pay of up to $10,000 more. Candidates must meet the requirements for medical officer, with experience in nutritional science, epidemiology or related fields. Contact Janet Gregory or Jerry Chambers, NCI Personnel Office, 301-496-6862.

CERVICAL CANCER-VIRUS STUDY WOULD SUPPORT EIGHT GRANTS, FIVE YEARS

(Continued from page 1)
the Board of Scientific Counselors of NCI's Div. of Cancer Etiology at the Board's recent meeting. The Board also approved the concepts of new contract supported initiatives with estimated annual costs totaling $2.2 million and of the recompetition of existing contracts with estimated annual costs totaling $4.2 million.

The papillomavirus cervical cancer study would fund as many as eight grants for five years, DCE Director Richard Adamson said. The concept came out of a workshop held earlier this year, chaired by Marcel Baluda, a member of the DCE Board. Staff description of the proposal follows:

"The consensus of the workshop participants was that the human papillomaviruses (HPV) were the strongest viral candidates for a major role in the etiology of cervical carcinoma. Several laboratories have demonstrated the presence of HPV DNA in both cervical carcinomas and dysplasias. In one study, 70-90 per cent of cervical tumors contained DNA from either HPV types 16 or 18. In addition, mild dysplasia appeared to be associated with the presence of DNA from HPV types 6 or 11. A number of established cervical tumor cell lines have been examined and found to possess DNA segments of HPV type 18. HPV antigens and cytological markers have also been detected in a large percentage of dysplasias examined. Other HPV types have been strongly associated with human laryngeal papillomas and the skin disease epidermodysplasia verruciformis. Various animal papillomaviruses are also known to transform cells in culture and to induce malignancies in their native hosts.

"The workshop participants noted, however, that little information was available on the expression and function of the HPV DNA found in the dysplasias and carcinomas and on the progression of the disease from primary infection to dysplasia or carcinoma. Studies are needed to determine the natural progression and transmission of HPV infections (e.g. does HPV infection always precede the development of dysplasia and/or carcinoma?); the expression and function of the associated HPV genome at various stages in the pathogenesis of cervical lesions; and the host response to such infections. These questions have not been answered due to a lack of basic information on the mechanisms of virus replication and oncogenic transformation. Suitable cell culture systems have not yet been found which could serve as models for these functions. However, the availability of recombinant DNA techniques should help overcome this impediment. Thus, it was consensus of the workshop participants that studies in all the above areas are needed. Such studies will help to elucidate the role of HPVs in the etiology of cervical cancer.

"The major emphasis of the basic research to be funded under this RFA will be studies on the molecular biology of HPVs and on the natural progression of HPV infection in its native host. Examples of such studies (which are not all encompassing) are (1) elucidation of the mechanisms of viral infection, replication and oncogenic transformation; (2) developlment of in vitro model systems using either wild type or genetically engineered HPVs; (3) functional and structural characterization of HPV encoded proteins with particular regard to pathogenicity and tissue specificity; (4) determination of the HPV types associated with specific categories of cervical lesions; (5) determination of the rates of regression or progression of cervical lesions in HPV infected subjects (these studies will not preclude the referral of human subjects for treatment when indicated by accepted medical criteria; (6) the nature of the host's response to HPV; and (7) the role of other viral agents, such as HSV or CMV, in the oncogenic process."

Alan Schreier is the program director.

Another major new initiative was reflected in the Board's approval of the concept for a contract, to cost nearly $1 million a year, for support services for biochemical epidemiology. It will be competed as a prime contract, with subcontracts to be awarded for individual projects. Descriptions of new contract concepts approved, with staff justifications, follows:

Title: Etiologic investigations of rare reproductive cancers. Estimated first year cost, $300,000, two years.

The Environmental Epidemiology Branch has an established program of research on a variety of cancers of the reproductive system and the breast. Studies are aimed at cancers that are relatively common as well as those that are less frequent. Among cancers of the reproductive system that have received limited epidemiologic attention are malignancies of the vulva and vagina. Both are rare cancers, the average annual age adjusted incidence per 100,000 women in the SEER areas in 1973-77 being 1.6 and 0.7 for cancers of the vulva and vagina, respectively. Both cancers are more common in older women as well as in blacks. Apart from these features, little is known regarding the etiology of either disease. Various risk factors have been suggested, but for the most part are based on clinical case series rather than carefully designed case control investigations. Among the postulated, although not established, risk factors for vulvar carcinoma are low socioeconomic status, obesity, vitamin A and E deficiencies, early age at menopause, smoking, hypertension, diabetes mellitus, infection and/or trauma related to poor personal

hygiene, promiscuity, and premalignant vulvar lesions. For vaginal cancers, the role of transplacental estrogens has been well documented among young women with clear cell adenocarcinoma. Among older women, who have mainly squamous cell tumors, some attention has been given to vaginal trauma, including pessaries or injuries at childbirth. Other unconfirmed factors are chronic leukorrhea, leukoplakia, chronic vaginitis, late menopause, obesity and douching practices.

Of recent interest is a reported increase in the incidence of in situ vulvar lesions, particularly among younger women. This parallels changes in sexual behavior, leading to speculation that vulvar cancer, like cervical cancer, may be caused by a sexually transmitted agent. Herpes simplex virus type 2 (HSV-2) has been identified in vulvar tumor tissue and many cases show serological evidence of prior herpes infection. Human papillomavirus (HPV) is known to cause genital wards (condyloma acuminatum) which have been followed by vulvar cancer in a substantial proportion of cases. Furthermore, in situ vulvar carcinomas have recently been found to contain HPV antigens. For vaginal cancers, no epidemiologic or laboratory investigations have been carried out to evaluate the role of infectious agents.

It has been suggested that different squamous cancers of the lower reproductive system may have common etiologic factors, particularly in view of similar demographic patterns (e.g. high rates in black women) and a tendency for multiple primary tumors involving these sites. For example, vaginal carcinomas are often diagnosed simultaneously with carcinomas of the vulva and cervix, as well as frequently a few years after hysterectomy for severe dysplasia or carcinoma in situ of the cervix. These observations have led to a theory of the multicentric origins of squamous cell carcinomas of the vagina, vulva, and cervix. Thus, epithelial malignancies of these sites may arise in response to the same etiologic factors; the older age range over which vulvar and vaginal carcinomas usually appear compared to cervical cancers may be due to the longer latency periods for these two sites, or to the action of cofactors or promotional agents. Since so little is known about the causes and mechanisms of either cancers of the vulva or vagina, there is a need for well designed case control investigations involving relatively large geographic areas and/or long time periods to accrue sufficient numbers of cases for study.

The objectives of this contract, which will combine research and support activities, are: (1) to identify environmental exposures of women that predict the risk of developing vulvar and vaginal cancers; (2) to relate serological indicators (e.g. infectious agents, micronutrients) to risk of thes0 cancers.

Ideally, this case control study would be population based in which cases represent all women over age 25 years with in situ and invasive vulvar and vaginal cancers in a defined geographic region and controls a sample of the general population of the same geographic area. If this design is not feasible based on RFP responses, the study will be hospital based with cases representing all vulvar and vaginal cancer cases diagnosed within a defined time period. In this circumstance, controls would be either hospital or neighborhood controls, determined by the referral patterns of eligible cases. It is anticipated that study subjects will be accumulated from several cancer registries or clinical centers, and that approximately 400 cases of vulvar cancer and 175 cases of vaginal cancer diagnosed over a two year period will be included. Approximately 800 control subjects will be selected in such a manner that they can serve as a common comparison group for both cancer sites. Both cases and controls participating in the study will be interviewed using standardized data collection forms developed by NCI. In conjunction with the interview, a small sample of blood will be requested from all study subjects for determination of serum antibody and micronutrient levels. It is anticipated that assays for herpes simplex virus types 1 and 2, serum carotene/retinol and tocopherol will be conducted under support from a separate contract. Additional sera will be frozen for future determination of papillomavirus antibodies. In addition, once the collaborating centers have been established, the logistics of obtaining fresh tumor specimens on a sample of cases will be assessed. This subsample of the total case series will be used to assess the frequency of papillomavirus infection.

Standard methods for analyzing case control data will be employed. These will include estimate of risks associated with various exposures. Since many of the factors will be highly correlated, multivariate analyses will be pursued to define independent effects.

Louise Brinton is the project officer.

Title: Case control study of cancer and drinking water contaminants. Estimated first year cost, $150,000, three years. (NCI will contribute an estimated $380,000 total to the project, EPA $70,000).

In 1975, chloroform and other halogenated organics were discovered in chlorine treated drinking water. Toxicologic and epidemiologic studies were mounted to evaluate possible risk to humans. Elevated numbers of kidney and liver tumors were observed in rodent feeding studies of chloroform. Epidemiologic surveys showed geographic correlations between site specific cancer mortality rates in U.S. counties and drinking water source and treatment. Case control studies using information from death certificates confirmed and extended these observations. The most consistent positive findings were for cancers of the bladder, colon, rectum, and brain. Pancreas, stomach, and lung cancers were also correlated with drinking water source, but less consistently.

Using data from a large case control interview study of bladder cancer, and information from an independent survey of water utilities, we have developed a methodology to explore associations between cancer risk and drinking water source. While there was no overall risk elevation among persons

using chlorinated surface water for long periods, selected findings from this study do warrant further evaluation. Among study subjects otherwise at low risk--nonsmokers who were never employed in a high risk occupation--bladder cancer risk increased with duration served by chlorinated surface water sources. In the study area with the most intense agricultural land use, bladder cancer risk among all risk groups increased with exposure duration to chlorinated surface water sources.

Objectives of this study and its contract are:

1. To determine the risk of incident cancers of the colon, rectum, bladder, brain, and pancreas associated with source of drinking water. Liver and kidney cancers will also be included, if feasible.

2. To replicate and refine observations from the National Bladder Cancer Study of associations, in an agricultural state, between bladder cancer risk and the use of a chlorinated surface source of water.

3. To evaluate the effects on cancer incidence of duration and latency of water related exposures, as well as the interaction of these exposures with other site specific risk factors, such as cigarette smoking and usual occupation.

4. To improve and refine models used to estimate past exposure to carcinogens in drinking water. The Environmental Protection Agency will collaborate with NCI in this part of the study.

A population based case control study using mailed questionnaires is planned of incident cancers of the colon, rectum, bladder, brain, and pancreas that occur within a defined geographic area with an existing population based tumor registry. The time period of diagnosis for eligibility will vary by cancer site to ensure adequate numbers and statistical power for each site. The geographic area will be selected to limit the ascertainment period for any one cancer to two years. The area must also have relatively low inmigration, and must have a variety of drinking water sources, including contamination free ground water and surface sources likely to have been contaminated with high levels of chlorination byproducts, pesticides, nitrates, and other potentially toxic compounds. Cases will total approximately 2,500, with 300-600 for each anatomic site. Fifteen hundred controls will be selected from the general population, frequency matched to the expected proportion of cases in strata specific for sex, race, and age. Controls less than 65 years of age will be selected by random methods and those 65 and older from a random sample drawn from Health Care Financing Administration rosters.

Data from residential histories will be merged at NCI with historical information on water quality to establish a lifetime exposure profile for each respondent. Standard methods for analysis of unmatched case control data will be used to evaluate risk for each site specific malignancy as related to drinking water quality. Risk will be evaluated for level, duration and latency of exposure as well as interaction with other risk factors. Water quality will be estimated by applying historical information about water supplies to statistical models that are based on recent measures of chlorination byproducts and other contaminants. The contract will be a research contract because of the need for a principal investigator who has experience in conducting epidemiologic studies, who has access to a population based tumor registry, and who is knowledgeable about water systems in the region.

The EPA (Health Effects Research Laboratory in Cincinnati) will collaborate with NCI in estimating past exposures. Current levels of trihalomethanes in drinking water supplies of the study area will be measured several times and compared with each other and with levels measured five years ago. Consistency of rank order among supplies will bolster confidence in extrapolating to historical levels for these contaminants. In addition, five representative water supplies will be studied intensively to determine the feasibility of estimating historical drinking water levels of pesticides and nitrates. Success in this effort will permit epidemiologic evaluation of these contaminants. EPA has agreed to contribute $70,000 to help defray expenses of environmental measurements. The EPA project officer will oversee environmental aspects of this project.

Kenneth Cantor is the NCI project officer, and Gunther Craun is the EPA project officer.

Title: Support services for biochemical epidemiology. Estimated first year cost, $940,488, four years.

In recent years there has been growing enthusiasm for incorporating the collection of biological specimens and the performance of laboratory studies into the design of epidemiological studies of cancer. These include studies of (a) viral serology and viral nucleic acid sequences in patients with or at risk of hepatocellular carcinoma, Burkitt's lymphoma, nasopharyngeal carcinoma and carcinoma of the uterine cervix; (b) hormones in breast and prostatic cancer; (c) micronutrients in cancers of the lung, larynx and urinary bladder; (d) carcinogen DNA adducts in persons exposed to environmental carcinogens, and antibodies to these adducts; and (e) bile acids, steroids and mutagens in colon cancer. The Epidemiology & Biostatistics Program and the Laboratory of Human Carcinogenesis (LHC) of NCI have a long standing interest in and involvement with this emerging new discipline, biochemical epidemiology, by virtue of its program of interdisciplinary studies in persons at high risk of cancer. In this context, the staff of the Environmental Epidemiology Branch (EEB), Clinical Epidemiology Branch (CEB) and LHC has accrued considerable experience in collecting, processing and storing biological specimens, and in applying virologic, cytogenetic, immunologic, immunogenetic, molecular and cellular sensitivity assays to the materials collected, in collaboration with appropriate laboratory scientists. Observations resulting from this work include: (a) characterization of the relationships between human T-lymphotropic virus (HTLV-1) and adult T-cell lymphoma (ATL), HTLV-3, hepatitis B virus, and acquired immune deficiency syndrome (AIDS); (b) demonstration that helper/suppressor cell ratios and acid labile alpha interferon are useful surrogate markers for AIDS risk; (c) the finding of benzo(a)pyrene DNA

adducts and antibodies to these adducts in persons exposed to this compound in the workplace and via tobacco smoke; (d) documentation of important relationships between the major histocompatibility complex (HLA) and familial susceptibility to Hodgkin's disease, hairy cell leukemia, and Waldenstrom's macroglobulinemia and to infection with HTLV-1; (e) identification of abnormalities in cellular response to carcinogens in families prone to sarcomas and to melanoma; and (f) description of a 3:8 chromosomal translocation in familial renal cell carcinoma. More recently, this approach has been applied by other investigators in the Epidemiology & Biostatistics Program. Current projects of this type include: (a) an assessment of serum micronutrients in a case control study of women with cervical cancer; (b) thyroid hormone measurements in a cohort of children irradiated for tonsillar hypertrophy; (c) quantification of cytogenetic abnormalities in various irradiated populations; and (d) a hepatitis B serosurvey in a study of primary liver cancer among World War II veterans. Additional opportunities to incorporate a biochemical and/or molecular component into epidemiologic investigations are widespread, and appear to offer great promise both as measures of cancer susceptibility and as indicators of carcinogen exposure. However, our ability to undertake such studies is constrained by the available resources, a lack of flexibility in expeditiously marshalling resources to test new etiologic hypotheses and lack of a systematic mechanism for obtaining the required services. In the past, program staff have had to locate appropriate resources for a particular study on an ad hoc basis, and once identified, initiate individual contract procurement processes that were often subject to delay and, when totalled, excessively costly. The availability of a single procurement mechanism through which efficient access to a wide range of high quality laboratory assays could be obtained would permit additional program initiatives in these areas. It would also provide for standardization of operation, increased quality control, and improved management and supervision.

EEB and LHC propose to procure support services for projects in biochemical epidemiology. We envision selecting a contractor with the following capabilities: (a) experience in the collection, shipment, processing and short term storage of a wide variety of biological specimens (including whole blood, serum, plasma, red cells, white cells, urine, feces and tumor tissue); (b) experience in the performance of laboratory work; (c) experience in monitoring and computerizing the accrual of laboratory data, particularly with reference to appropriate use of quality control procedures; and (d) an extensive subcontracting capability, by means of which a broad range of serologic, hematologic, bacteriologic, virologic, molecular, enzymatic, micronutrient and exposure related assays can be purchased. The final requirement is needed since the wide range and diversity of assays required makes it unlikely for any one laboratory to provide high quality laboratory support for all the tests required. The responsibility for collecting epidemiologic (interview) data would not belong to the proposed contractor. This would be handled through other program resources. As a resource contract, the laboratory assays sought would be only those which are available on a service basis. No developmental work would be procured with this mechanism. While it is expected that the contractor will have some capability to send specimen collectors into the field, under most circumstances the cost of specimen collection will be built into the budget of each specific study. Thus, ordinarily, the contractor's responsibilities would begin with the logistics of specimen transfer from the field to a central processing and short term storage facility. Long term specimen storage would be handled under an existing contract, through which EEB already maintains a computerized biospecimen repository. The management of this contract will be shared between EEB and LHC. EEB and LHC will each provide a coproject officer to oversee the procurement. Proposals to incorporate a biochemical component into newly planned epidemiologic studies will be reviewed by, and require approval from, a six member committee comprised of three senior investigators from each branch. This panel will be supplemented on an ad hoc basis by NCI scientists with appropriate specialized areas of expertise, as required by the proposals under consideration. Furthermore, aside from the projects listed below, we plan to bring to a committee of the DCE Board of Scientific Counselors for approval all biochemical epidemiology projects with estimated costs exceeding $100,000. The following studies are being planned during the initial two years of this contract:

1. Biochemical epidemiology of lung cancer. A pilot case control study of lung cancer is planned, which would include 100 newly diagnosed, untreated cases and 200 matched controls. Its goal would be identifying those specific laboratory assays which appear to hold promise in clarifying the biochemical epidemiology of lung cancer. Study participants would be interviewed to obtain the usual demographic information, data related to factors thought to influence the assays, a detailed smoking history and a review of potentially carcinogenic environmental/occupational exposures. Among the assays to be evaluated are carcinogen modified DNA in lymphocytes; serum antibodies to tobacco smoke related carcinogen DNA adducts; carcinogen DNA adducts in urine; DNA repair enzyme activity in lymphocytes; urinary polynuclear aromatic hydrocarbons; drug metabolism phenotyping; and urinary cotinine to monitor exposure to tobacco smoke.

More specialized studies are planned for lung tissue specimens (both normal and neoplastic) which are obtained from cases at the time of surgery. These assays will be performed inhouse by LHC intramural laboratories, and include assays of oncogene expression, carcinogen activation, and measurements of DNA repair enzyme activity in both neoplastic and normal lung tissue.

2. Biochemical studies in tumors which occur excessively in blacks. As a laboratory adjunct to the series of population based case control studies of those cancers which occur excessively in black

Americans (approved by the Board last June), biochemical assays will be performed to characterize differences in blacks and whites, and when possible, cases vs. controls. The following are planned: pancreatic cancer (1100 cases and controls), Lewis blood group type; prostate cancer (800 cases and controls), hormones, nutrients and viruses; multiple myeloma (700 controls only), quantitative immunoglobulin profiles; esophageal cancer (600 controls only), nutrients.

3. Viral studies in U.S. women with carcinoma of the uterine cervix. A case control study of cervical cancer is currently under way in five U.S. comprehensive cancer centers. Blood specimens are being obtained from a sample of 500 cases of invasive cancer, 300 women with in situ carcinoma and 1,000 controls, with the primary focus being upon serum micronutrients. Prediagnosis blood samples are available on approximately 125 women. This study will be expanded to include serologic assays for herpes simplex virus type 2, and human papillomavirus (when a reliable test is available).

4. Laboratory studies in Oriental American women with breast cancer. A population based, case control interview study of Chinese, Japanese and Filipino American women (600 cases and 1200 controls) with breast cancer is being planned among residents of San Francisco, Los Angeles and Oahu. Blood and urine samples will be obtained from study participants to assess nutrients and hormones.

5. Urine mutagens and carcinogen DNA in truck drivers. Several epidemiologic studies have documented an excess of urinary bladder cancer in truck drivers, an association that is independent of smoking status. Exposure to motor exhaust fumes has been suggested as a possible source of carcinogenic exposure in these men, with a leading hypothesis being that diesel exhaust fumes represent the critical exposure. Experimental support for this hypothesis is derived from the fact that nitropolycyclic aromatic hydrocarbons are potent mutagens which occur at higher levels in diesel compared with nondiesel exhaust fumes. A pilot study is under consideration in which nonsmoking truck drivers who are exposed to (a) diesel fumes; (b) nondiesel fumes; and (c) no recent motor exhaust exposure, will be interviewed and provide a urine sample to determine if mutagenicity and/or presence of carcinogen DNA adducts correlate with type of exposure.

6. DNA adducts in long term survivors of Hodgkin's disease. From the original NCI cohort of 198 patients with Hodgkin's disease treated with combination chemotherapy (MOPP) with or without radiation, 62 of 91 survivors have been examined and have donated bone marrow as part of an attempt to identify subclinical morphologic functional and cytogenetic abnormalities which might characterize persons at increased risk of treatment related acute leukemia. These samples will be evaluated for the presence of DNA chemotherapy adducts.

7. Exposure measurements in workers exposed to solvents. The Occupational Studies Section of EEB is currently conducting two large cohort studies of workers with occupational exposures to potentially carcinogenic solvents--dry cleaners exposed to perchloroethylene, Hill Air Force Base aircraft mechanics exposed to 1,1,1 trichloroethane. We plan a pilot study designed to test the feasibility of quantifying solvent exposures by measuring solvent levels in the blood and seeking the presence of DNA damage in blood lymphocytes. A small sample of study subjects will be drawn from each of the two cohorts for each of several solvent exposure levels as determined by work history interviews and air measurements.

8. Exposure measurements in workers exposed to pesticides. The Occupational Studies Section is currently studying several large cohorts of workers with occupational exposures to potentially carcinogenic pesticides--structural pest control workers exposed to organochlorine (especially chlordane), organophosphate and carbamate pesticides; and grain millers and handlers exposed to organochlorine compounds (especially ethylene dibromide). Using a pilot approach similar to that outlined for solvent workers, an attempt will be made to measure chlordane and EDB levels in blood and to seek the presence of pesticide DNA adducts in blood and urine in an exposure stratified sample of workers from each of these two cohorts.

9. Laboratory studies in Latin American women with cervical cancer. The Environmental Studies Section is planning a combined epidemiologic/laboratory study of 800 Latin American women with invasive cervical cancer and 1600 controls. Also to be studied are the husbands of 400 sexually monogamous cases and 800 similar controls. Under a previously approved concept and contract, funds have been provided for assays of herpes simplex virus type 2, carotene and retinol in sera obtained from study participants. Under this proposed contract, funds would be provided to support specimen shipment from the field and specimen processing, and for conduct of additional assays of interest, particularly human papillomavirus, when a reliable serologic assay becomes available. Tumor tissue will also be obtained for molecular studies.

10. Biochemical studies of oral cancer. A multicenter case control study of oral and pharyngeal cancer has been initiated (supported by another contract) to evaluate etiologic hypotheses regarding chewing tobacco, diet, mouthwash use, and occupation. The proposed contract would support a biochemical component to supplement the data obtained by interview, and would assess chromosal damage in exfoliated oral cells for several categories of individuals via the micronucleus test, a procedure which has helped identify persons at high risk of oral cancer in other populations; and evaluate severity of disease upon blood levels of certain nutrients and possibly viral antibody titres, and conduct case control comparisons if extent of cancer

(Continued on page 8)

DCE ANNOUNCES RESOURCES AVAILABLE

The Div. of Cancer Etiology of NCI prepared the announcement on page 7 describing resources it is making available to the scientific community.

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

has not influenced the blood levels.

11. Biochemical epidemiologic studies in China. A series of case control studies of cancer are under way in high risk areas of China. Etiologic factors for cancers of the esophagus, lung, stomach and choriocarcinoma are being assessed via interview and laboratory study funded by a contract with the Cancer Institute of the Chinese Academy of Medical Sciences. Support from the proposed contract would supplement the existing effort in two ways--by providing for replication of certain assays to assist in quality control, and by providing for additional assays that cannot now be reliably conducted in China.

Mark Greene and Dean Mann are the project officers.

"This is a well conceived project," Board member Hilary Koprowski commented. "It is long overdue."

"This will be of terrific assistance to intramural research," Board member Gilbert Omenn said. "Would this knowledge be useful to extramural investigators? Can we make it available to all principal investigators and prospective applicants? This will advance the whole initiative of biochemical epidemiology. I think it is important to share this."

Greene said the information would be made available to anyone.

"The epidemiology branches are in an unfair situation," Board member Myron Essex said. "Wet labs can change directions by purchasing new materials by transferring supplies money from one area to another. When epidemiology takes a new direction, it has to be presented as new research."

(More concepts approved by the DCE Board will appear in next week's issue of **The Cancer Letter**).

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CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY: RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

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RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CN-55443-10
Title: Operations office for inter-institutional nuclear magnetic resonance (NMR) studies.
Deadline: Jan. 4

NCI's Div. of Cancer Prevention & Control is soliciting proposals from organizations interested in establishing an NMR operations office to organize a network of NMR laboratories to carry out research in the detection and diagnosis of cancer. It is the intent of this contract to initiate inter-institutional studies among NMR laboratories which are already contributing to cancer research. This proposed procurement is subject to the availability of funds.

Contract Specialst: Joan O'Brien
RCB Blair Bldg Rm 2A01
301-427-8745

NCI CONTRACT AWARDS

TITLE: Preparation of monoclonal/monospecific antibodies to oncogene products of avian and mammalian retroviruses
CONTRACTOR: Scripps Clinic & Research Foundation, $1,885,246.

TITLE: Application of the human tumor colony forming assay to new drug screening
CONTRACTORS: Univ. of Arizona, $809,985; Univ. of California (Los Angeles), $596,656; and Mayo Foundation, $687,700.

TITLE: Collection, storage, quality assurance and distribution of biological response modifiers
CONTRACTOR: Meloy Laboratories, $1,232,251.

TITLE: Partial support of Institute of Laboratory Animal Resources
CONTRACTOR: National Academy of Sciences, $185,000.

TITLE: Tracing individuals for environmental epidemiologic studies of cancer using vital statistics records
CONTRACTOR: Westat Inc., $75,000.

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