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SENATE SUBCOMMITTEE OKs $850 MILLION FOR CANCER; NCI REVEALS HOW IT WOULD SPEND FISCAL 1978 FUNDS

The Senate HEW Appropriations Subcommittee last week approved $850 million for NCI in the 1977 fiscal year, an increase of $77 million over the amount in the House bill.

The $773 million approved by the House Appropriations Committee would have, as NCI Director Frank Rauscher said, "put us into a holding pattern for at least a year," with virtually no funds for new initiatives or program growth.

(Continued on page 2)

In Brief

LAWSUIT COULD DELAY DIET-NUTRITION CREGS; HUGH DAVIS REPLACES MERCADO AS CIB CHIEF

MEMBERS of the National Assn. of Life Sciences Industries (NALSI) an organization of for-profit (or tax paying, as they prefer to be known as) firms have threatened legal action against NCI award of Cancer Research Emphasis Grants unless the restriction against the award of grants to private industry is lifted. Gio Gori, director of the Diet, Nutrition & Cancer Program, told the DNCP Advisory Committee that such a lawsuit might delay award of the first round of CREGs in the program, now undergoing review. Gori had hoped the awards would be made prior to Sept. 30, permitting funding with fiscal 1976 money. A member of the association, however, told ***The Cancer Letter*** that it is not likely the group would go that far. "Legal action has been mentioned as a last-ditch alternative, but I don't think it will reach that point," he said. There's no legislative fiat against grants to private industry; it's an HEW regulation which could be changed by an order of the secretary. . . . **THERE WERE** 110-115 applications for the diet and nutrition CREGs, Gori said. They're competing for six grants. FY 1976 funding for the program will be somewhat under the $6 million originally allotted, from $5 to 5.5 million. . . . **RAUL MERCADO** has left as chief of NCI's Clinical Investigations Branch to become chairman of the newly-established Dept. of Radiation Oncology at St. Louis Univ. Hugh Davis is new CIB chief; he's on a two-year leave from the Univ. of Wisconsin. . . . **ERNEST PARK** Jr., president of Microbiological Associates, was recently elected NALSI president. John Landon, president of EGG-Mason Research Institute, is vice president; Orrie Friedman, president of Collaborative Research Inc., is treasurer, and Katharine Noll, Hazleton Laboratories, is secretary and assistant treasurer. Howard Brown Jr. was reelected vice president and executive director. Donald Nielsen, president of Hazleton, was reelected chairman of the board; other board members include Robert Fennell, Electro-Nucleonics Laboratories; J. Leslie Glick, Associated Biomedic Systems; Thomas Li, Biotech Research Laboratories; Thomas Murchison, Dawson Research Corp., and James Nance, Litton Bionetics.

NCI TO TELL NCAB HOW IT WOULD SPEND $955 MILLION, $1.07 BILLION IN 1978

(Continued from page 1)

Unless the $850 million figure is changed when the bill reaches the Senate floor, the final figure after the usual compromise between the two houses would give NCI about $810-815 million. That still would not be as big an increase over the previous year ($763 million for fiscal 1976) as NCI has enjoyed regularly since 1971, but it would save the program from the stagnation built into the House bill.

The final figure will also be considerably less than NCI had asked in its budget submission to the White House—$948 million.

An appropriation in the $810-815 million range will permit NCI to fund up to 40% of approved competing grant applications—combined renewals and new grants. At the House figure, only 30% could be funded, compared with 47-49% in FY 1976.

· The Senate subcommittee added $216.5 million for all of NIH over the House bill, bringing the total for NIH to $2.644 billion.

With the appropriation for the 1977 fiscal year, which starts Oct. 1, still far from settled, NCI will present to the National Cancer Advisory Board next week budget projections for the 1978 fiscal year. Those projections describe a program based on a "mid-level" appropriation of $955 million and another based on an "upper-level" figure of $1.073 billion.

The billion-dollar estimate is probably not realistic at this point, considering that NCI's 1977 appropriation will be around $815 million. Even the $955 million may be too much to expect. But NCI put together some convincing justification for both the mid and upper level figures, broken down by program:

A. Cause and Prevention Research

1. Epidemiology. Mid-Level—Increase of 9 positions and $3.9 million over the 1977 estimate of 73 positions and $17.9 million.

Epidemiology studies to identify environmental and other factors responsible for clusters of high risk communities would be expanded. Additional field research designed to test etiologic hypotheses would be pursued. Research to determine the interactions between familial and genetic factors and environmental factors in the development of cancer would be conducted. The epidemiology of breast cancer would be pursued to determine the correlation of steroid-binding characteristics of breast cancer with epidemiologic risk factors, as well as the relationships of exogenous hormones and other environmental agents to breast cancer incidence. Studies would be initiated regarding smoking and alcoholism as high-risk factors in head and neck cancer and the effectiveness of antismoking and antidrinking clinics in reduction of risk. Studies to identify populations exposed to known and suspected occupational environmental bladder carcinogens would be pursued.

Upper-Level—Increase of two positions and $2.7 million over the mid-level estimate.

The program of collaborative studies with other agencies that possess important epidemiologic resources which require active involvement and coordination by NCI would be expanded. Studies would be pursued into the underlying reasons for variations in cancer patterns in domestic animals and their possible association with human disease. Types of neoplasia for which epidemiological relationships have not been adequately characterized (e.g., pancreas, brain, biliary tract) would be investigated. Methods for large scale definitive studies requiring collection of new data including laboratory determinations would be developed and tested. The interrelationships of inherited and environmental contributions to high risk for large bowel cancer would be studied.

2. Carcinogenesis (Physical and Chemical). Mid-Level—Increase of 13 positions and $12.8 million over the 1977 estimate of 189 positions and $95.4 million.

The in vitro carcinogenesis program would be expanded. Additional bioassay testing of substances for carcinogenic potential in animal systems would be done. The extent and rate of development of carcinogenesis information systems would be expanded. Growth of programs devoted to the pathogenesis of those cancers having major human impact but for which no good experimental model systems are available would be continued. Activity of this program in the fields of lung cancer, pancreas cancer and others have been highly productive and can be extended to the fields of endocrine cancers, digestive tract cancers and childhood cancers. Studies on carcinogen chemistry, metabolism and toxicity would continue to expand. An increased effort would be made to define the interaction of viruses and biological, physical and chemical factors (environmental carcinogenesis) resulting in the transformation of cells of malignancy. Research designed to provide greater acceptability of cigarettes now believed to be at or below the threshold for cancer risk and respiratory damage due to smoking would be pursued. Studies involving modification of host response to chemical carcinogens and sunlight would be pursued. Animal models of head and neck cancer using known head and neck carcinogens would be established.

Upper-Level—Increase of 12 positions and $15.7 million over the 1978 mid-level estimate.

The possible use of dietary, hormonal, and other means of protecting individuals against the effects of exposure to environmental carcinogens would be explored. Increased efforts would be made in in vitro carcinogenesis screening, for additional bioassay testing and for the further development of new and improved testing programs and methodologies.

Increased effort would be made on the pathogenesis of major cancer types and on the inhibition of

their development, with emphasis on applicability of inhibition methods to man. A major coordinated program designed to elucidate the information required to make informal evaluations of human risk would be created. More realistic attention would be paid to the question of how to safely handle carcinogenic substances in the laboratory. Research into areas beyond the fundamental information on the complex events involved in the interaction of biological, physical and chemical factors resulting in transformation of cells to malignancy would be pursued.

3. Viral Oncology. Mid-Level—Increase of eight positions and $7.4 million over the 1977 estimate of 311 positions and $99 million.

High quality viral diagnostic reagents needed to conduct studies in human populations at high risk to breast cancer would be produced. The identification and isolation of the sequence(s) responsible for transformation would be expanded, as well as continued studies into understanding the formation of DNA transcript of the virus. Events that follow the integration of viral genes into the genetic materials of host cells would be analyzed as well as the search for a protein product of viral genes possibly responsible for transformation. Continued effort would be made to counteract or suppress the malignant properties of transformed cells so that they are once again subject to normal growth control, e.g., by chemicals—natural or synthetic—that induce differentiation.

Upper-Level—Increase of seven positions and $9.3 million over the 1978 mid-level estimate.

Tests would be conducted to determine whether a given DNA virus is a possible agent of human cancer by looking for its DNA in the cancer cells. The genomes of tumor-inducing viruses to determine the position, structure and function of their constituent nucleic acid sequences would be analyzed, as well as the mechanism of integration of viral genes into the cell genome and their excision therefrom.

4. Nutrition. Mid-Level—Increase of one position and $2.4 million over the 1977 estimate of four positions and $5.2 million.

Oral nutrient solutions would be evaluated in addition to the development of improved ones. Existing oral nutrient solutions would be studied for deficiencies in nutrient composition for specialized needs as well as patient acceptability. Evaluation would be done on the use of dietary survey techniques and procedures in populations selected on the basis of cancer incidence and dietary habits. New studies would be initiated to determine the effect of dietary antioxidants on spontaneous and chemically induced cancers, the role of diet and nutrition on carcinogen-metabolizing enzymes.

Upper-Level—Increase of one position and $1.8 million over the 1978 mid-level estimate.

Efforts would be initiated to define host-tumor competition for nutrients. Laboratory studies of certain implicated dietary components would be pursued. Additional studies would explore the role of selenium as a modifier of cancer incidence, and the effect of carcinogens on different strains of rats in relation to diet.

5. Immunology. Mid-Level—Increase of one position and $574,000 over the 1977 estimate of two positions and $4.1 million.

Studies would be pursued to determine the basis for increased incidence of lymphomas and certain other tumors in immunologically abnormal animals. The mechanism underlying increased tumor incidence following viral-infection of immunosuppressed animals would be further explored. A postulated tumor promoting effect of immune response under special circumstances would be investigated. A new systematic approach using a cell culture system to determine if the immune system normally removes potentially malignant cells (immune surveillance) would be initiated.

Upper-Level—Increase of $375,000 over the 1978 mid-level estimate.

The cell culture system approach to the study of immune surveillance using coordinated in vivo and in vitro test systems would be expanded. The development of large scale studies of cancer incidence in humans with immunologic abnormalities would be pursued.

B. Detection and Diagnosis Research

1. Epidemiology. Mid-Level—Increase of six positions and $3 million over the 1977 estimate of 40 positions and $9.2 million.

Studies would be conducted to determine why many cancer patients have advanced disease at first presentation, e.g., socio-cultural, ignorance, fear, and host defense mechanisms. The development of specialized registries would be initiated which would contain information on persons with genetic defects, and on persons exposed to certain contaminants. The Surveillance, Epidemiology, End Results Reporting (SEER) Program would be expanded.

Upper-Level—Increase of two positions and $1.1 million over the 1978 mid-level estimate.

Expanded research would be conducted on potential screening and diagnostic tests for forms of cancer that usually give little advance warning prior to being diagnosed as metastatic disease.

2. Tumor Biology. Mid-Level—Increase of $5,000 over the 1977 estimate of $87,000.

3. Immunology. Mid-Level—Increase of one position and $1.4 million over the 1977 estimate of 62 positions and $12.6 million.

Immunodiagnostic tests currently in clinical use would continue to be refined. Research would be conducted to identify promising new human tumor antigens and possible development of new immunodiagnostic tests. Development of multidisciplinary approaches to the serologic and chemical characterization of promising new human tumor antigens would be encouraged. Clinical studies would be sup-

ported to determine the usefulness of new immunodiagnostic tests.

Upper-Level—Increase of $853,000 over the 1978 mid-level estimate.

Support would be provided for the development of immunoassay techniques. Studies on T, B, and null cell immune responses would be conducted as well as studies of humoral antigens in relation to pancreatic cancer. Immunochemical studies of prostatic acid phosphatase would be supported.

3. Diagnostic Research. Mid-Level—Increase of three psotions and $4.5 million over the 1977 estimate of 135 positions and $29.2 million.

Research would be supported to follow up the finding that the carcinogenicity of asbestos depends on fiber shape (long, thin fibers cause cancer); improve radiologic methods for cancer diagnosis, including x-rays and ultrasound, with emphasis on computer-assisted imaging; determine cost effective methods for mass screening; standardize multidisciplinary diagnostic research protocols; improve biopsy techniques for pancreatic cancer; and define and clarify genetic syndromes associated with a high incidence of large bowel cancer.

Upper-Level—Increase of eight positions and $4.9 million over the 1978 mid-level estimate.

The collection and registry of cancers of marine animals would be expanded; these represent "sentinels" of the contamination of water by industrial carcinogens. Funds would be used to improve x-ray

would be initiated. It would attempt to demonstrate the feasibility of using nutritional supplementation in support of traditional modes of cancer treatment to increase the survival rate and improve the quality of cancer patient life during and after therapy.

Upper-Level—Increase of $1 million over the 1978 mid-level estimate.

The hyperalimentation program would be expanded and extended into the cause and effects of anorexia in adult and pediatric patients. The interrelationship of anorexia, cancer type, treatment modality and associated phenomena would be explored.

3. Tumor Biology. Mid-Level—Increase of one position and $413,000 over the 1977 estimate of seven positions and $2.2 million.

Upper-Level—Increase of $41,000 over the 1978 mid-level estimate.

4. Immunology. Mid-Level—Increase of three positions and $2.3 million over the 1977 estimate of 14 positions and $22.2 million.

Model studies would be started on new immunotherapeutic approaches, stressing mechanisms of action rather than simply the testing of new agents according to various schedules. Research would continue to define the mechanism of action of immunotherapy.

Upper-Level—Increase of $2 million over the 1978 mid-level estimate.

Research into the application of BCG and other

The drug development program would be expanded to include the systematic evaluation of fungi for their potential to produce antineoplastic agents, the resynthesis of selected compounds and the analysis and preparation of selected large-scale chemical compounds.

Increased emphasis would be given to studies relating to the selectivity of drug action including the development of precise methods for identification of specific cell functions and kinetic aspects of cell proliferation.

A spectrum of animal and human (xenograft) tumors as a new secondary screen has been established. Input of agents is to consist of agents passing initial or "pre-screening" in vivo or in vitro, active natural product isolates, and material with activities of pertinence reported from other programs. An expansion of this program is required as candidates for spectrum screening are already exceeding 1,000 per year with 4,000 agents on file as candidates. In addition, the incorporation of human tumor xenografts as models for specific human tumors is needed for more realistic, sensitive, and clinically extrapolative test systems for detection and preclinical evaluation of new agents.

The current tumor screening spectrum would be modified and expanded, as well as new systems being developed to include such important tumors as ovarian, pancreatic, and bladder; evaluation of such screens as phage, erythroleukemia, cell surface-lectin phenomena, lytic and deaminase inhibitors as tests for fermentation both to ascertain if new antineoplastic agents can be obtained, as well as exploration of novel approaches for a pre-screen to detect mutagenic agents; expansion of the screening effort for anti-viral activity in vivo; and, implementation of a literature surveillance system to identify compounds displaying biological activity, as a source for the screening programs.

A radiation toxicology program would be initiated to develop early predictions of late effects of radiotherapy.

A synthetic program to develop active radiation sensitizer agents would be established.

It is now possible to measure DNA damage produced in cells after treatment with DNA-damaging agents at therapeutic doses. It is proposed to measure the sensitivities of normal and neoplastic cells or tissues to these agents and to correlate the DNA damage produced with therapeutic effects in animals and ultimately in man. This could provide a predictive sensitivities test for particular neoplasms. It is further proposed to examine combinations of agents, at least one of which is of the DNA-damaging type. From these latter studies, particular combinations and timing of agents could be proposed. Along similar lines would be a systematic study of inhibitors of RNA and DNA polymerase for anti-viral and antitumor activity which may lead to effective inhibitors of latent tumor viruses and possibly of tumors as well.

Recent research results have indicated that humans acquire RNA tumor viruses. The DNA provirus was specifically highly related to the endogenous RNA type-C virus of baboons. It is believed this finding indicates an interspecies transmission of virus some time in the past. One of the components of the virus reported isolated from one AML patient was highly related to the baboon virus. New information now needed includes: (a) a widespread molecular epidemiology study looking for this virus information in many tissues of many people—normal and with neoplasias, including the study of Asians and Africans; and (b) the determination if any particular expression of this information (DNA back to RNA) correlates with maintenance of the transformed state. Both objectives are readily technically achievable.

Research studies on proper sequencing of chemotherapeutic agents would be expanded. Due to modifications of new experimental drugs, assays of hormonal chemotherapeutic combinations in vivo interdependent of multiple chemotherapeutic agents are carried out.

Central tissue culture facilities are needed in order to continue to pursue research on the effects of hormones on breast cancer cells, bone marrow cultures, hyperthermia and methotrexate action and toxicity in tissue culture.

Additional projections for preclinical treatment research and for the remainder of NCI's programs will appear in ***The Cancer Letter*** *next week.*

ABSTRACTS OF OUTSTANDING PAPERS PRESENTED AT ANNUAL AACR MEETING

The program committee for the 67th annual meeting of the American Assn. for Cancer Research selected 44 papers as among the outstanding ones presented at the meeting. The following abstracts are from that list, chosen from sessions on biology, immunology, chemical carcinogenesis, biochemistry, and experimental chemotherapy. This concludes publication of the 44 abstracts in ***The Cancer Letter.***

ESTABLISHMENT OF A HUMAN CEA-PRODUCING COLON CARCINOMA LINE AND ITS RESPONSE TO ANTITUMOR AGENTS – L.Y. Yang, B. Drewinko, and M.M. Romsdahl, M.D. Anderson

A line (LoVo cells) derived from human colon carcinoma tissue has been propagated for over two years. Cells grow in monolayers, display acinar structures, and form colonies with a plating efficiency of 40%. Kinetic parameters of exponentially growing LoVo cells are: doubling time, 37 hr; generation time, 30 hr; and growth fraction, 90%. CEA synthesis is accomplished primarily by cells in stationary phase of growth while expoentially growing cells produce negligible quantities. Release of CEA is independent of phase of growth. LoVo cells exposed to increasing doses of ionizing radiation show a threshold-type survival curve with D_q and D_o values similar to those of other human lines. Recovery from sublethal damage was demonstrated in fractionated exposure experiments. Survival curves for LoVo cells treated with increasing concentrations of adriamycin show a continuous exponential decrease. Survival of hydroxyurea treated cells decrease exponentially to a plateau of 45%. Ftorafur and 5-fluorouracil show similar theshold type survival curves but ftorafur appears significantly more effective.

Our data indicate that LoVo cells constitute an excellent in vitro model to investigate mechanisms of CEA synthesis and to define lethal effects of drugs potentially useful in the treatment of colon carcinoma.

IDENTIFICATION OF A NEW GROUP OF POTENT INDUCERS OF DIFFERENTIATION IN MURINE ERYTHROLEUKEMIA CELLS – Robert Reuben, Richard Wife, Ronald Breslow, Richard Rifkind and Paul Marks, Columbia Univ.

Induction of erythroid differentiation in murine erythroleukemia cells (MELC) can be achieved by many small molecular weight compounds containing a localized dipole moment. One such compound, N-methylacetamide, was dimerized by linkage through varying numbers of methylene groups in order to determine the optimal distance between functional groups and increase the effective concentration of inducer at adjacent hypothetical binding sites. Acetamide dimers linked through 2 to 8 methylene groups were tested. All such bisacetamides were active as inducers. The 5 to 8 carbon linkage was optimal for minimum effective concentration (0.2mM) and maximum induction (>99%). Hexamethylene bisacetamide (HMBA), n=6, was active at concentrations 1/6 that of the monomer, N-methylacetamide. The dimer of N-methylacetamide, n=2, was no more active than N-methylacetamide alone, demonstrating the necessity for a minimum separation of functional groups. Related natural diamines, e.g. cadaverine, were weak inducers. With 5mM HMBA, the extent of differentiation as judged by % cells induced, extent of hemoglobinization, and erythroid morphology was greater than with any other inducer yet tested. Thus, a new chemical series, bisacetamides, are potent inducers of differentiation of MELC.

LYSOLECITHIN ANALOGS: A NEW CLASS OF IMMUNOPOTENTIATORS WITH ANTITUMOR ACTIVITY – Paul Munder, Herbert Fischer, Hans Weltzien, Herbert Oettgen, and Otto Westphal, Max Planck Institute & Univ., Freiburg, Germany, and Memorial Sloan-Kettering

Different immunologic adjuvants activate phospholipase A in macrophages. This results in conversion of cellular lecithin to lysolecithin (LL) which has adjuvant activity and has been considered as a possible common pathway of adjuvant action. As its half-life is short, we have synthesized analogs (LLAs) with the aim of augmenting the immunopotentiating effect of LL. Various ester-deoxy-, ether-arylkoxy-, and either-deoxy-LLAs, have been tested in the mouse and some were found to (1) increase the production of antibody to sheep red cell antigens and soluble protein antigens, (2) inhibit the growth of Ehrlich ascites carcinoma inoculated IP into NMRI mice and (3) inhibit the growth of methylcholanthrene-induced BALB/c sarcoma Meth A inoculated IP or SC into (BALB/c x C57BL/6F$_1$ mice. Inhibition of tumor growth was achieved by systemic administration (IV or SC), beginning at the time of tumor inoculation or after the transplant was established. After complete regression of sarcoma Meth A, mice were resistant to further transplants of the same tumor.

We conclude that synthetic LLAs are effective immunopotentiators, and may be useful in cancer therapy.

CARCINOGEN EFFECTS OF GLUCOCORTICOID NUCLEAR BINDING IN RAT LIVER – Thomas Kensler, William Busby Jr., Nancy Davidson, and Gerald Wogan, MIT

Treatment of rats with a number of chemical carcinogens, (e.g., AFB$_1$, DMN) blocks glucocorticoid induced synthesis of liver tyrosine aminotransferase and tryptophan pyrrolase. The induction process is mediated by glococorticoid binding to cytoplasmic receptors and interaction of these glucocorticoid-receptor complexes with nuclear acceptor sites altering the transcription of specific parts of the genome. Using glucocorticoid binding as a probe of chromatin function, the ability of [^{3}H]-dexamethasone-cytosol receptor complexes to bind to rat liver nuclei prepared from 100 g adrenalectomized male Fisher rats treated with various chemicals was investigated. The apparent concentration of nuclear binding sites (p moles [^{3}H]-dex. bound/mg DNA); measured by incubating at 0°C [^{3}H]-dexamethasone-cytosol receptor complexes with nuclei isolated from the same rats significantly diminished following sublethal AFB$_1$, DEN, DMN, TAA, 3-MC, 3'Me-4-DAB, 4-DAB, and actinomycin D treatment. AFB$_2$ and acetaminophen were without effect on the kinetics of the binding reaction.

Time course and dose-response experiments utilizing AFB$_1$ suggest that these observed effects on reduced glucocorticoid binding capacity are not attributable to non-specific effects of cellular necrosis.

ENZYMATIC MARKERS OF MALIGNANT TRANSFORMATION – George Weber, Robert Jackson, and Noemi Prajda, Indiania Univ.

The purpose of this work was to identify enzymatic markers of malignant transformation by examining the behavior of key enzymes in a spectrum of liver tumors of different malignancy. In all hepatomas, irrective of malignancy and growth rate, marked alterations were found in specific activities of 10 key enzymes. Enzyme activities increased in pentose phosphate synthesis, glucose-6-phosphate dehydrogenase (2-44-fold), transaldolase (1.5-3.4-fold); in de novo purine biosynthesis, glutamine PRPP amidotransferase (1.5-3.2-fold); adenylosuccinase (1.4-2.2-fold); and in IMP ultilization, adenylosuccinate synthetase (1.6-3.7-fold); IMP dehydrogenase (2.8-13-fold). In contrast, in the purine catabolic pathway, xanthine oxidase and uricase decreased 2-10-fold. In pyrimidine metabolism the enzyme leading to DNA and RNA biosynthesis, UDP kinase, increased 1.7-4-fold, whereas the catabolic enzyme, thymidine phosphorylase, decreased 3-fold. Similar alterations were observed in transplantable rat kidney tumors and in human primary hepatomas and kidney tumors. These alterations are specific to neoplasia, as no such change was observed in differentiating or regenerating liver.

Since this reprogramming in gene expression occurs in all tumors examined so far, it is concluded that it appears to be linked with the malignant transformation itself and the enzymes are markers of malignancy. The alterations confer selective advantages to the cancer cells.

METABOLIC REQUIREMENTS FOR THE LETHALITY OF BLEOMYCIN IN E. COLI – Seymour Cohen, Univ. of Colorado

The bleomycins are antitumor agents composed of various polyamine amides of a common inactive bleomycinic acid. At 1 µgm per ml at 37° the spermidine derivative of bleomycin (A5) was far more lethal to E. coli than four other bleomycins tested. An exponential loss of viability was produced for several hours in a synthetic medium. In stringent E. coli, strain 15 TAU RC^{str}, withholding thymine did not affect the rate of killing. Uracil starvation completely blocked bleomycin killing. Arginine deprival partially inhibited bleomycin killing in the stringent cell but had little effect on the lethality of bleomycin in a relaxed isogenic strain actively synthesizing RNA. The lethality of the antitumor agent, bleomycin, which is reported to produce breaks in bacterial and animal cell DNA in vivo and in vitro, appeared totally dependent on RNA synthesis in E. coli.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg. NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NO1-CP-65816-12

Title: *Computer-aided prediction of metabolites for carcinogenicity studies*

Deadline: *Aug. 2*

NCI is interested in creating a computer-based resource which can predict probable metabolites of chemicals. This project can aid in the identification of unknown substances isolated in metabolic studies and in the study of structure-activity relationships in carcinogenicity as well as aid in the selection of chemicals for the bioassay.

Contract Specialist: Dorothy Britton
Cause & Prevention
301-496-6361

RFP EPA-DU-76-B229

Title: *In vitro screening of selected air pollutants for potential carcinogenicity-detection of genotoxic effects of environmental chemicals in cultured liver cells*

EPA expects to award a contract to develop and test in vitro systems for assessing potential carcinogenicity via the quantitative assay of genotoxic effects such as DNA breakage, repair and mutagenic effects of enviromental effluent chemicals potentially emitted from alternative energy sources. The proposed research will utilize mammalian liver cells in culture which contain metabolic capability to activate procarcinogens.

RFP EPA-DU-76-B245

Title: *In vitro screening of selected air pollutants for potential carcinogenicity using microbial systems*

EPA expects to award a contract for the purpose of integrating analytical chemical techniques with those of microbial mutagenesis bioassay in screening selected air pollutants for potential carcinogenicity. The successful contractor shall be expected to collect representative air samples consisting of particulate and vapor phase components. Samples shall be tested for mutagenic activity using selected strains of Salmonella typhimurium and then fractionated by methods which yield component mixtures compatible with further bioassay and analytical techniques for identification of the potentially carcinogenic components in the sample. Methodology employed shall provide the capability of giving qualitative and quantitative results in both bioassay and chemical analysis programs and shall lend itself to becoming a routine standardized procedure.

Environmental Protection Agency
Contracts Management Div. (MD-33)
Attn. NCCM-L
Office of Administration
Research Triangle Park, N.C. 27711

Contract Awards

NCI RACES TO BEAT CONTRACT DEADLINE THAT NO LONGER EXISTS

Award announcements poured out of the NCI Research Contracts Branch last week as contracts personnel labored to beat a deadline that no longer exists. The federal government's fiscal year end date of June 30 has been moved to Sept. 30, effective with the current, 1976 fiscal year. In recent years, the Contracts Branch had to obligate funds made available as late as mid-April before the June 30 deadline; ordinarily, money not obligated by the fiscal year end reverts to the Treasury.

NCI decided not to take advantage of the extra three months this year in obligating most of its contract funds, thus giving contractors the benefit of that extra time. Some CREG and other grant awards will not be made until September, permitting final review by the National Cancer Advisory Board at its September meeting.

Largest award announced last week was to Biospherics Inc., Rockville, Md. firm, for technical writing and telephone answering services in response to cancer related inquiries, nearly $1.2 million. The Univ. of Chicago received an award of $466,012 for evaluation of information requirements for image processing of cell samples as a basis for development of an automated cell recognition system.

Other large awards went to Litton Bionetics, $837,581, for monitoring of immunologic competence in cancer patients; Montefiore Hospital, $717,-956, for studying psychological aspects of breast cancer; Univ. of Hawaii, $418,150, for collection of indigenous and exotic plants; and Harlan Industries, $441,720, for production of athymic (nude) mice.

Litton Bionetics received a modification of its current contract of $493,854 for additional alterations and renovations at the Frederick Cancer Research Center. That brought the total for the current contract year, which ends June 26, to $24,495,493 for both the science programs and alterations and renovations. The cumulative total for converting the Army biological warfare center to cancer research since Litton was awarded the contract in 1972 is now $69,925,161.

Litton has 15 more months with the present contract, which has been renewed annually without competition. NCI will issue an RFP is August to recompete the contract.

Other awards:

Title: Role of stroma in the growth of neoplastic and preneoplastic lesions of the mammary gland
Contractor: Baylor College of Medicine, $95,000.

Title: Biochemistry of normal and tumor cell surface antigens
Contractor: Univ. of Alabama, $52,144.

Title: Role of macrophages in tumor immunology
Contractor: Univ. of Minnesota, $76,313.

Title: Quantitative assays of monocyte-macrophage function
Contractor: Robert B. Brigham Hospital, Boston, $110,000.

Title: Randomized evaluation of C. parvum as an adjunct to chemotherapy in disseminated carcinoma of the breast
Contractor: Sloan-Kettering Institute, $110,627.

Title: Evaluation of levamisole as a therapeutic adjunct in squamous cell carcinoma of the head and neck
Contractor: Sloan-Kettering Institute, $88,782.

Title: Cancer immunotherapy: Phase I study of effects of immune stimulants on human immune response
Contractor: Mayo Foundation, $91,450.

Title: Immunotherapy in outbred cat lymphoma and leukemias
Contractor: Harvard College, $64,183.

Title: Stimulation or suppression of immunologic responses
Contractor: Univ. of Chicago, $63,700.

Title: Macrophage assay for malignant disease
Contractor: New York State Dept. of Health, $26,368.

Title: Detect animal carcinoma antibodies for human studies
Contractor: The Wistar Institute, $70,260.

Title: Development of immunodiagnostic tests for cancer
Contractor: Robert B. Brigham Hospital, Boston, $59,424.

Title: Detection and localization of bronchogenic carcinoma
Contractor: Mayo Foundation, $153,920.

Title: Suppression of endocrine function by systemic agents as treatment of human breast cancer
Contractor: Hershey Medical Center, $65,645.

Title: Study for an operation impact evaluation system at NCI cancer centers
Contractor: CDP Associates, La Jolla, Calif., $93,347.

Title: Study of effector molecule binding to mammary cell surfaces
Contractor: Stanford Univ., $124,000.

Title: Application of breast pump to obtain breast secretions
Contractor: Univ. of California (San Francisco), $10,950.

Title: Research into the control of DNA synthesis in the mammary gland
Contractor: Stanford Univ., $90,000.

Title: Study into biochemical mechanism of endocrine induced breast cancer regression
Contractor: Univ. of Texas Medical School (San Antonio), $120,000.

Title: Study of growth alteration of mammary neoplastic cells obtained by manipulation of cellular environment
Contractor: Univ. of Texas Medical Branch (Galveston), $95,100.

Title: Biochemical nature of hormone dependency in breast cancer
Contractor: Univ. of Chicago, $120,000.

Title: Study basic biological events in the pathogenesis of mammary cancer
Contractor: New York State Dept. of Health, $82,200.

Title: Procurement of sulfolipids from mycobacterium tuberculosis strain H37RV
Contractor: National Jewish Hospital & Research Center, Denver, $48,047.

Title: Cervical cancer screening
Contractor: Arkansas Dept. of Health, $202,154.

Title: Diagnostic applications of human tumor or organ-associated antigens
Contractor: Univ. of Washington, $100,685.

Title: Active specific immunotherapy in acute myelogenous leukemia
Contractor: UCLA, $87,782.

Title: Biochemistry of normal and tumor cell surface antigens
Contractors: Univ. of Wisconsin, $68,935; Fred Hutchinson Cancer Research Center, $60,297.

Title: Specific and non-specific immunotherapy as an adjunct to chemotherapy in skeletal and soft tissue carcinomas
Contractor: UCLA, $146,642.

Title: Antibodies to human tumor cells
Contractor: Univ. of Southern California, $86,300.

Title: Selective stimulation or suppression of humoral or cellular immunologic responses
Contractor: Yale Univ., $72,400.

SOLE SOURCE NEGOTIATIONS

Proposals are listed here for information purposes only. RFPs are not available

Title: Characterization of the nucleic acids of the avian myeloblastosis virus
Contractor: Massachusetts General Hospital.

Title: Study of high risk breast cancer families
Contractor: Michigan Cancer Foundation.

Title: SEER and Third National Cancer Survey Data Processing Services
Contractor: Geomet Inc., Gaithersburg, Md.

Title: Development and application of N-nitroso compounds and their precursors in the environment
Contractor: British Foods Manufacturing Industries Research Assn.

Title: Implementation of a comprehensive plan for developing cooperative action and common practices among cancer institutes
Contractor: Assn. of American Cancer Institutes.

The Cancer Letter—*Editor* JERRY D. BOYD

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