THE CANCER LETTER

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REGIONAL GROUPS: WHY 15 WERE NOT AMONG THOSE FUNDED; CANCER REGIONAL STUDIES REVIEW COMMITTEE CHARTERED

The fact that only two new regional cooperative groups scored well enough in review to be funded when NCI had set aside enough money to support three came as a bitter blow to the 15 other groups which competed and a lesser disappointment to the advocates of the regional

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In Brief

NEW CANCER CONTROL PROGRAMS ON SCHEDULE; NCI EXPECTS 10-15 CCRU, 30-40 CCSP APPLICATIONS

NCI'S NEW THRUST in cancer control—dropping cancer center outreach grants and replacing them with Cancer Control Research Unit and Cancer Control Science Program grants—is on schedule, with a mid-August deadline for applications in both areas. Div. of Resources, Centers & Community Activities staff screened about 65 letters of intent, expects to get 10-15 CCRU and 35-40 CCSP applications. Who will do the review has not yet been determined, probably will require two ad hoc groups. NCI plans to award five grants in each program, if applicants score well enough in review. . . . **ANDREW HEGYELI**, program director for carcinogenesis in DRCCA's Occupational Medicine Branch, died June 6 at a Bethesda hospital following a heart attack. He was 62. A native of Hungary, Hegyeli earned two doctorates, one in veterinary medicine and the other in comparative anatomy, embryology and general pathology at Palatinus Josephus Univ. in Budapest. He came to the U.S. after fleeing Hungary during the 1956 revolution. . . . **PETER MAGEE**, Fels Research Institute director, will continue one more year as chairman of the Board of Scientific Counselors of NCI's Div. of Cancer Cause & Prevention. Magee's term on the Board was due to expire with last month's meeting but an exception was obtained to keep him on. Other members of the DCCP Board whose terms have expired are Ingegerd Hellstrom, Brian Henderson, George Klein, Warren Nichols, Barry Pierce, Louis Siminovitch, James Watson, and Bernard Weinstein. Commenting about his service on the Board, Pierce said, "I've never been on a committee that's had such excellence of staff work. The realization that we were being paid attention to, to a university professor, came as quite a blow. Dr. (Richard) Adamson (DCCP director) listened not only to our decisions but to the tenor of the discussions. That has made this one of the finest associations I've ever had." . . . **NIH DIRECTOR** James Wyngaarden has made his first major appointments. Lester Salans, who has been acting director of the National Institute of Arthritis, Diabetes & Digestive & Kidney Diseases, had "acting" removed from that title. Mortimer Lipsett, director of the NIH Clinical Center, was named director of the National Institute of Child Health & Human Development.

WHY 15 REGIONAL GROUPS DID NOT MAKE IT; NEW REVIEW COMMITTEE CHARTERED

(Continued from page 1)

group concept among NCI staff members and their advisors.

The two successful groups were the Piedmont Oncology Assn., headed by Charles Spurr with the Bowman Gray School of Medicine Oncology Research Center as the core institution, and the Mid-Atlantic Oncology Program, headed by Philip Schein with the Georgetown Univ. Lombardi Cancer Research Center as the lead institution.

Five others were approved by the study section, the ad hoc review group sometimes called "CCIRC B." Ten were disapproved.

The competition among new regional groups for NCI support was set up when the Board of Scientific Counselors of the Div. of Cancer Treatment, with NCI Director Vincent DeVita's strong support, decided after its extensive review of clinical trials that more regional groups were needed (there already were two—the Northern California Oncology Group and the North Central Cancer Treatment Group).

DCT earmarked $1.5 million a year to fund up to three new groups. Somewhat less than that will be utilized by the two which were funded.

Disappointment over the failure of more new groups to compete effectively was lessened to some extent by the advent of the Community Clinical Oncology Program. While CCOPs will not be expected to function in the same manner as regional cooperative groups, they will make clinical trials available to greater numbers of patients on a more widely distributed basis, which were among the goals of regional groups.

Regional groups, including the new ones, will be eligible to serve as research bases for CCOPs.

Disappointment still exists among the new groups which were left unfunded, however. It is possible that they will get a second chance. The National Cancer Advisory Board asked the DCT Board to consider issuing the RFA again, and the Board agreed to take that up at its October meeting.

Would those groups do better the second time around? Not only would they be competing against each other once again, but they might be facing competition from still other new groups. In any event, they at least know now what their weaknesses were, as perceived by the study section. Among those deficiencies were:

- Unrealistic expectations on patient accrual, or failure to document claims of anticipated patient accrual. This was the most common deficiency. Patient accrual is a problem with all cooperative groups and probably was the major factor in those failures which have occurred among established groups in recent years.
- Failure to demonstrate that groups were more than "paper organizations." Some applications came in which listed institutions as members that had no track record whatever of working together. In some cases, applications failed to include even letters of commitment from members agreeing to participate in group activities.
- Deficiencies in the science. Studies proposed in some applications were not imaginative or original, in some cases were not well thought out and were deficient in some aspects of protocol design. Some groups either lacked members with sufficient scientific expertise to carry out clinical trials or failed to document that that expertise was available. In some instances, facilities either were lacking or were not documented as being available.
- Apparent lack of interchange among members. Some applications gave the appearance that group activities would be nothing more than an "outreach program," with protocols generated by the lead institution and disseminated to the members with no opportunity for two way interchange in their development.

"The biggest problem was the numbers," John Killen, NCI project officer for regional groups, commented. "Failure to document that the resources required to carry out the studies proposed were available was another."

Reviewers frequently could see that, from the size of the hospitals in the group, projections of patient accrual were not realistic.

Regional cooperative groups fall roughly into two categories—one, built around one university or free standing cancer center with the other members consisting of community hospitals, clinics, VA hospitals, or smaller university associated hospitals; the other, associations of two or more university based or free standing cancer centers along with a lesser number of small institutions. North Central and Piedmont are in the first category, NCOG and Mid-Atlantic the second.

A plurality of the 17 groups was along the lines of the first category, but there was no pattern as far as deficiencies were concerned—they were evident in equal amounts in both categories.

If the regional group RFA is reissued, correction of the deficiencies which appeared in the first round obviously would profit those reapplying, as well as other groups which might be organized.

Those groups interested in trying again, along with other new groups, do not necessarily have to wait for reissuing the regional group RFA. They may compete at any time in the regular cooperative group cycle. They would be up against some very stiff competition from the established groups which may be coming up for renewal at the time their applications are reviewed. In competing under the rubric of an RFA, new groups would not be head to head against existing groups.

Reorganization of the clinical trials review groups in NCI's Div. of Extramural Activities has been completed with the formal chartering of the new Cancer Regional Studies Review Committee.

The new committee will review all regional cooperative groups and most of the disease or anatomically oriented groups. The Cancer Clinical Investigation Review Committee will continue to handle the national and multidisciplinary groups, the two pediatric groups, the Radiation Therapy Oncology Group and the Gynecologic Oncology Group.

The new committee will have a lesser workload for the time being, but as the former contract supported groups come up for renewal, that workload will increase. The committee will start with a "core" of eight permanent members, with ad hoc members added as needed to suit the requirements of groups being reviewed.

Dorothy Macfarlane has been executive secretary of both CCIRC and the ad hoc committee, and will continue "for the present" as exec sec of the new committee. Members of the new committee have not yet been appointed and will not necessarily include those who have served on the ad hoc committee.

This week's meeting of the CCIRC was the last as chairman for Joseph Simone, associate director for clinical research at St. Jude Children's Research Hospital. The new chairman will be William Donegan, professor of surgery at the Medical College of Wisconsin. Other members whose terms have expired are Alfred Bartolucci, Univ. of Alabama (Birmingham); Clara Bloomfield, Univ. of Minnesota; Hugh Davis, Henry Ford Hospital; and Richard Kempson, Stanford Univ.

CONGRESSIONAL BUDGET RESOLUTION INCLUDES ADDITIONAL MONEY FOR NCI

The 1983 fiscal year budget resolution so laboriously and painfully worked out by Congress, finally agreed upon last week, included the Heflin amendment which added $22 million to the amount originally agreed upon by the Senate Budget Committee for NCI (*The Cancer Letter,* June 4).

The new total places NCI's fiscal 1983 budget at $986.6 million. President Reagan's request was $955.5 million, only $12 million more than NCI is getting in the current fiscal year. The Senate Budget Committee had lifted that to $966.6 million. The final budget resolution which came out of the House-Senate conference left the Heflin total in.

The amendment by Sen. Howell Heflin (D.-Alabama) would give NCI an extra $115 million over the next three years. Those are anything but hard figures, however. In the first place, next year's budget resolution will start the process all over again, subjecting the 1984 and 1985 amounts to new revisions. In the second place, the budget resolution only sets spending goals. Congress has committed itself to stay within the total government wide figure, but even that is subject to change. The various appropriations committees have their individual bills, with funds for each agency, yet to consider. They can manipulate the intradepartmental figures around as they see fit. They can go under or over the totals established by the budget resolution if they can get the votes to support changes.

Having the additional money in the resolution is better than not having it, however. It demonstrates that Congress still is more enthusiastic about the National Cancer Program than is the White House, whatever the party which controls either. Even if Congress does appropriate $986 million or something close to it, rescision or deferral requests still pose a threat. But there is a very good chance that NCI will get $30 million more than in the Presidential budget, and that would take some of the pressure off, permit the funding of a few more R01s, save some of the threatened program projects, perhaps make more money available for centers, construction, and cooperative groups.

The Heflin amendment authorizes $1.026 billion for FY 1984, $71.4 million less than requested in the bypass budget approved in May by the National Cancer Advisory Board. The bypass budget will go directly to the White House without change by NIH or HHS. However, the budget the President will submit to Congress next January will limit NCI to a total developed by the department, which is completely contrary to the language of the National Cancer Act.

The 1984 bypass budget would fund all grants at their recommended levels, all National Research Service awards with 100 percent of the institutional allowances, and would fund all competing grants to the 180-185 payline. All those categories are being funded at less than recommended levels to the 185 payline (so far) in the 1982 fiscal year.

The FY 1984 bypass budget would fund only about 25 percent of approved competing grants.

One aspect of the 1984 budget breakdown by mechanism shown on page 4 which should be pointed out is that the amount for "organ systems" has been drastically reduced from amounts shown in previous years. The figures here represent estimates for a headquarters grant only, with the rest of the money (as high as $17 million in previous years) placed in the regular research grants column. That reflects the NCAB's decision to consolidate the four Organ Site Project headquarters into one and to require that future Organ Site Program grants be competed as R01s, program projects or clinical research cooperative agreements (program project and cooperative agreement columns here do not include any of the estimated transfers).

Another item which shows up in the bypass budget every year and is always decimated in the White

NATIONAL CANCER INSTITUTE 1984 BYPASS BUDGET

MECHANISM GROUP TABLE (Dollars in Thousands)

	1982		1983 (President's Budget)		1984		1983 1984
	Amount	% of Total	Amount	% of Total	Amount	% of Total	% Change
Group I – Investigator-Initiated							
Regular Research Grants	$253,733	37.5%	$258,643	37.8%	$ 309,310	39.3%	19.6%
Program Projects–P01s	106,713	15.8	109,063	16.0	115,327	14.6	5.7
Clinical Education Program	5,800	.9	6,000	.9	7,000	.9	16.7
Research Career Program	4,973	.7	4,973	.7	5,500	.7	10.6
Fellowships	22,799	3.4	22,065	3.2	28,500	3.6	29.2
Organ Systems	627	.1	688	.1	750	.1	9.0
Cancer Centers Core Support	74,062	10.9	76,924	11.3	83,900	10.7	9.1
Cooperative Agreements	43,973	6.5	45,029	6.6	49,316	6.3	9.5
Subtotal	512,680	75.8	523,385	76.6	599,603	76.2	14.6
Group II – Co-Initiated							
Request for Applications (RFA)	14,464	2.1	17,748	2.6	18,847	2.4	6.2
Research Contracts	31,587	4.7	24,825	3.6	27,114	3.5	9.2
Subtotal	46,051	6.8	42,573	6.2	45,961	5.9	8.0
Group III – NCI/NCP Initiated							
Resource Contracts	99,449	14.7	103,962	15.2	108,817	13.8	4.7
Interagency Agreements	13,997	2.1	11,886	1.8	12,631	1.6	6.3
Subtotal	113,446	16.8	115,848	17.0	121,448	15.4	4.8
Group IV – Other Resources							
Construction Grants	1,000	.1	1,000	.1	17,000	2.1	1600.0
Construction Contracts	3,500	.5	1,000	.1	3,000	.4	200.0
Subtotal	4,500	.6	2,000	.2	20,000	2.5	900.0
Total	**676,677**		**683,806**		**787,012**		**15.1**
% of Total NCI Budget		**71.8**		**71.6**		**73.3**	
In-House Research	109,781	11.6	113,442	11.9	117,934	11.0	4.0
Management and Support	105,439	11.2	107,636	11.2	115,754	10.8	7.5
(NIH Management Fund)	(46,929)	(5.0)	(47,798)	(5.0)	(51,500)	(4.8)	(7.8)
Cancer Control (Grants, Contracts)	51,132	5.4	50,565	5.3	53,300	4.9	5.4
Subtotal	266,352	28.2	271,643	28.4	286,988	26.7	5.7
Total, NCI	**$943,029**		**$955,449**		**$1,074,000**		**12.4%**

House submission to Congress is the money for construction grants. This is an area where the meddlers at NIH and Office of Management & Budget place their expertise in determining the needs of the Cancer Program over that of the NCI director and the National Cancer Advisory Board. In most other categories, they permit NCI Director Vincent DeVita to allocate NCI's budget as he and his advisors see fit. But they shoot down construction every year, arguing that construction has a low priority government wide and NCI should be no exception. Never mind the results four years ago of the NCAB survey which showed that institutions involved in cancer research needed $25 million a year for five years just to bring their facilities up to federal and local code standards.

Accompanying the bypass budget to the White House will be a narrative describing how the money would be spent in each program area. The narrative includes projects which will be carried out even if NCI does not get all the bypass budget seeks, most of those at reduced levels of activity. It also describes projects which will not be undertaken without the substantial increase in funds. In the days of the Carter Administration's "zero based budget," the breakdown among those projects which would be funded at each level of funding was clear; now, it is more difficult.

A portion of the narrative follows, with the rest to be published in next week's issue:

I. Research

A. Epidemiology–Increase of $5,928,000 over the 1983 estimate of $56,248,000.

–Detailed analysis of cancer incidence, mortality, and survival data in populations covered by the SEER program will be carried out, and a new registry to cover more blacks and hispanics will be included.

NATIONAL CANCER INSTITUTE 1984 BYPASS BUDGET
RESEARCH PROGRAM STRUCTURE (Dollars in Thousands)

	1982	(President's Budget) 1983	Increase	1984	1983 1984 % Change
I. Research					
Epidemiology	$ 55,411	$ 56,248	$ 5,928	$ 62,176	10.5%
Carcinogenesis (Physical & Chemical)	92,124	94,735	7,650	102,385	8.1
Biological Carcinogenesis	88,539	85,804	8,916	94,720	10.4
Nutrition	16,311	17,244	2,245	19,489	13.0
Tumor Biology	110,283	114,898	13,584	128,482	11.8
Immunology	75,056	71,981	8,666	80,647	12.0
Diagnostic Research	37,231	37,716	5,540	43,256	14.7
Preclinical Treatment Research	144,634	149,969	14,503	164,472	9.7
Clinical Treatment Research	150,022	153,829	13,738	167,567	8.9
Rehabilitation Research	1,293	1,462	-724	838	-46.3
Subtotal	770,904	783,986	80,046	864,032	10.2
II. Resource Development					
Cancer Centers Support	75,711	78,618	7,347	85,965	9.4
Research Manpower Development	34,766	34,269	8,281	42,550	24.2
Construction	5,269	2,728	18,093	20,821	663.2
Subtotal	115,746	115,615	33,721	149,336	29.2
III. Cancer Control	56,379	55,848	4,784	60,632	8.6
Total, NCI	**$943,029**	**$955,449**	**$118,551**	**$1,074,000**	12.4%

—Case-control studies of selected cancers and populations in communities which are identified by cancer maps will continue.

—Occupational studies will be expanded through selected cohort and case-control studies that assess the carcinogenic hazards indicated by clinical, experimental, or epidemiologic observations.

—Efforts to identify the effects of low level radiation exposures and to promote collaboration with institutions that have special resources to evaluate radiation hazards will receive more emphasis.

—Risks of new cancers resulting from therapy with cytotoxic drugs will continue to be monitored by wider utilization of NCI sponsored clinical trials.

—Epidemiologic studies in collaboration with laboratory investigators will be intensified to evaluate the role of infectious agents in certain cancers such as Kaposi's sarcoma and T-cell leukemia.

—Multidisciplinary projects combining epidemiologic and experimental approaches will continue to receive special emphasis in order to evaluate causative factors that continue to elude detection by traditional epidemiologic methods.

—Urgent issues including those of regulatory or public policy concern will continue to be evaluated and developed for epidemiologic studies.

—Studies on family cancer syndromes and mechanisms of host susceptibility will receive increased emphasis.

—Updating of cancer maps will be emphasized using data for the 1970s, along with special analyses of time trends in cancer incidence and mortality, and surveys of cancer patterns among various racial and ethnic groups in the U.S.

—The determinants of racial differences in cancer patient survival will be examined.

—Case-control studies to evaluate the causes of rare cancers, involving collaboration of several centers and registries, will be emphasized.

—Surveillance of health effects of tobacco products on humans will continue and be complemented by chemical analysis of major smoke components in the newer domestic cigarettes.

B. Chemical and Physical Carcinogenesis—Increase of $7,650,000 over the 1983 estimate of $94,735,000.

—Specific genes regulating normal epithelial differentiation will be identified and altered expression in these genes during early stages of carcinogenesis will be characterized.

—The mechanism(s) by which chemical carcinogens alter gene expression during oncogenesis will be determined and the genetic determinants for susceptibility or resistance to the carcinogenic process will be examined.

—Biochemical and immunological analysis of enzymatic mechanism of carcinogen activation and detoxification will continue.

—Monoclonal antibodies will be developed for genetic analysis of drug and carcinogen metabolism, and for epidemiologic investigations to identify "high risk" individuals.

—Develop mechanisms for preventing the development of bladder cancer through studies of factors interfering with metabolism of carcinogenic agents or with the pathogenic processes leading to tumor development.

—Elucidate the biochemical control factors in normal and malignant colon cells to provide a molecular definition of process(es) at fault and thereby a sound scientific basis on which to identify methods for the prevention, control, and treatment of this disease.

—The stability of genetic information in normal and tumor cells will be examined using shuttle vectors, plasmids that replicate in both mammalian and prokaryotic cells. These shuttle vectors with specific genetic markers will be employed to analyze the effects of carcinogens on the genetic regulation of mammalian cells.

—The relationship of DNA repair and human cancer in tumor cells and cells from individuals that are cancer prone will be examined; the clinical, cellular and molecular basis of three human cancer prone genetic diseases (xeroderma pigmentosum, ataxia telangectasia, and familial malignant melanoma) with features of hypersensitivities to environmental agents will be defined.

—Deficiencies in DNA repair processes that contribute to cell- and age-specific susceptibility to chemical carcinogens will be identified.

—Cocarcinogenesis models in human and nonhuman cell and organ culture systems will be developed.

—Comparative carcinogenesis studies will be performed in the following pairs of cell culture systems: (a) human cells; epithelial vs. fibroblasts; (b) experimental animal cells; epithelial vs. fibroblasts; (c) epithelial cells; human vs. experimental animal; and (d) fibroblasts; human vs. experimental animal.

—Studies on chemical carcinogenesis in nonhuman primates will continue, with particular emphasis on the carcinogenic potential of antineoplastic and immunosuppressive agents, environmental contaminants and artificial sweeteners.

—Highly specific inhibitors of cytochrome P-450 catalized carcinogen activation which can modify the carcinogenic process will be developed.

—Contributory factors in transplacental, perinatal and pregnancy associated carcinogenesis will be examined, including emzyme induction phenomena in maternal, fetal, and placental tissues and inhibition of neoplastic expression by cellular differentiation.

—Studies on the isolation and characterization of cell surface receptors for tumor promoters will be performed and endogenous compounds, such as hormones, which activate the receptor for tumor promoters and thus may act as natural tumor promoters will be identified.

—Studies of the normal exocrine pancreas will be supported as a basis for the study of pancreatic cancer. Additional work is needed to document the incidence of spontaneous pancreatic tumors in experimental animals, and a search for chemicals which produce pancreatic adenocarcinoma will be continued.

—Nonphorbol tumor promoters present in the human environment will be identified, and studies on their mechanisms of action performed; development of nonphorbol tumor promotion models in human and in nonhuman cell and organ culture systems will continue.

—Mechanisms by which retinoids alter normal epithelial differentiation and act as inhibitors of chemical carcinogenesis and tumor promotion will be analyzed; studies on the effects of new synthetic retinoids in prevention of breast, bladder, and other cancer in experimental animals will continue.

—The ability of beta carotene to prevent the development of cancer in various target sites in experimental animals will be investigated. Various routes of administration of carotene will be studied, since this compound is absorbed poorly by many species of animals.

—Experimental evaluation of antioxidants and other selected chemical and biological agents as inhibitors of carcinogenesis will be performed and the mechanism(s) of action of effective molecules examined; studies on the role of free radial inhibitors/scavengers in anticarcinogenesis will continue.

—Studies on the mechanism of malignant transformation of cultured human bronchial cells by carcinogens and cocarcinogens in tobacco smoke will continue.

—New studies will be initiated on the pharmacological role of nicotine and the search continued for new markers which could be used for prediction of tobacco related disease in humans.

—Studies will continue on the toxicology of selected constituents in cigarette smoke with particular emphasis on tobacco specific nitrosamines.

—The role of transforming growth factors during normal embryogenesis and wound healing will be studied since peptide growth factors involved in normal wound healing and embryological development may be expressed to an excessive degree in malignant cells.

—Efforts to isolate and characterize transforming growth factors and to develop antagonists to them such as the retinoids, steroids and other potential chemopreventive agents will continue.

—Efforts to identify and characterize natural carcinogens which may be present in the diet will be continued.

—Short-term tests for identifying new inhibitors of

carcinogenesis present in food and natural products will be developed.

—Studies of conditions which contribute to the formation of mutagens/carcinogens in foods will be performed and alternate methods of food processing and cooking evaluated.

—Studies on the incidence of mutations, specific tumors and birth defects in humans exposed to ionizing radiation at low doses and low dose rates from external sources and internally deposited radioisotopes will be initiated.

—Studies on the effect of low dose radiation on the developing embyro and fetus in producing postnatal neoplasia will be initiated.

—Studies of specific radiation induced chromosomal abnormalities in cancer will be initiated to increase our knowledge of the relationship between radiation induced aberrations and radiogenic cancers.

—Resources to provide qualified investigators with fresh human tissues, frozen, freshly obtained human tissues, and derivative cell cultures, for use in cancer research will be developed.

—A chemical repository facility for the provision of well characterized chemical carcinogen reference standards to the scientific community will be operated and maintained. Synthesis will be carried out of selected chemical carcinogens, analogs and metabolites for use in cancer research as authentic standards for reference. Synthesis of radioactive retinoids used as tracers in metabolic studies, for pharmacokinetic investigations in vivo, and for investigations into the mechanisms of action of retinoids will also be performed.

C. Biological Carcinogenesis—Increase of $8,916,000 over the 1983 estimate of $85,804,000.

—New studies will be initiated on elucidating the relationship between human cytomegalovirus and human tumors such as Kaposi's sarcoma and prostate adenocarcinoma.

—Identification, isolation, and characterization of onco genes directly from human tumors will receive emphasis; methods to generate monoclonal antibodies against transforming onc genes of mouse and human origin will be developed.

—The recombinational events in the envelope gene of various endogenous leukemia viruses and the role of such permuted sequences as signals for blastogenesis will be examined relative to the c-regions of retroviruses.

—Emphasis on studies to determine the association of retroviruses in human disease will be increased, especially the biological, chemical and immunological characterization of the retroviruses recently isolated from human T-cell lymphomas and leukemias.

—Nature of promoting and activating sequences in retroviruses and papovaviruses will be compared by mutual exchange mechanisms. The number of such divergent elements capable of gene activation will be expanded.

—The association of EBV with lymphoproliferative diseases in immunocompromised and immunodeficient humans will be evaluated.

—The role of papillomaviruses in human benign tumors and in malignant processes will be studied.

—Studies to define the role of hepatitis B virus in primary hepatocellular carcinoma will receive greater emphasis.

—The mechanisms of transformation of hematopoietic and epithelial cells in tissue culture will be examined.

—Characterization of the cell derived transforming genes of retroviruses and studies on the mechanisms by which these genes cause neoplasia will be performed.

—The biochemical event responsible for the increased ATP utilization noted in several viral and chemically induced transformation systems will be investigated, with the objective of identifying its relationship to the malignant state.

—A detailed analysis using appropriate mutations of the nature of a new type of activator element and the nucleotide sequences (structures) which determine the level at which it performs will be undertaken; attempts will be made to isolate activator elements which may be present within the structure of eukaryotic chromosomes and would therefore be crucial to the control of hormone stimulated tumors.

—Those elements will be identified (at the nucleotide sequence level) which are responsible for binding of the hormone receptor complex to DNA and the subsequent enhanced expression of this set of genes. This will provide an insight into hormone regulated gene expression as well as the control of hormone stimulated tumors.

—Greater emphasis will be placed on development and application of sensitive assays for selected transforming and other growth factors useful for the screening of tumor patients (tissues, serum, urine) to aid in diagnosis, classification and prognosis.

—Attempts to define tumor specific antigens and synthesis of monoclonal antibodies directed against them for application to diagnosis, screening and immunotherapy programs will continue; studies on development and use of monoclonal antibodies against human colorectal carcinoma for diagnostic purposes will receive greater emphasis.

—The role of viruses and the immune system in modifying the carcinogenic process will be studied.

—Attempts will be made to detect viral proteins expressed on malignant cells and to define the immune defense mechanism involved in the destruction of such cells using monoclonal antibodies.

—The mechanism of tolerance and tumor immunity will be investigated, and the factors related to recognition of the self versus foreign antigens will be

determined using both cDNA and geonomic clones of the mouse major histocompatibility complex, H-2.

–The mechanism of action of various transforming proteins will be studies and will include the protein kinase activity of the src, p60, the various gag-x polyproteins, and several of the papovavirus T antigens.

–Transforming genes have been isolated from a number of human tumors by using the DNA transfection method. Two of these have been found to be homologous to viral onc genes. The extent and the spectrum of such genes is critical.

–Attempts to understand and isolate human homologues of known animal retroviruses by DNA cloning techniques, to show their potential infectivity and to study human promoter elements will continue.

–Artificial onc genes will be tailored consisting of various cellular sequences conjoined to assorted viral promoters to study the nature, location, and the distances requisit to turning on of cellular genes.

–Nutrition–Increase of $2,245,000 over the 1983 estimate of $17,244,000.

–Case control and cohort epidemiology studies will be intensified to clarify the role of dietary fat, fiber, micronutrients, food additives, and other dietary patterns in cancer etiology.

–Descriptive data on dietary patterns in different populations of the U.S. will be analyzed with respect to etiologic hypotheses of cancer.

–Methodologic studies will be pursued to optimize collection and analysis of dietary information through direct interview and biochemical measurements.

–Biochemical and molecular probes will be integrated with epidemiologic approaches to identify the dietary constituents and mechanisms involved in carcinogenesis.

–Case control studies in high risk and low risk areas will be continued to identify dietary factors responsible for geographic variation.

–Case control studies in migrant groups to the U.S. will be continued to clarify the changes in life style and diet that might be responsible for the changes in cancer rates.

–Prospective studies of populations whose nutritional status has been characterized will be continued.

–Areas of the world with exceptionally high rates for certain cancers will serve as the focus for case control studies and intervention studies.

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, citing the RFP number. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair Building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

RFP NCI-CM-37557

Title: *Large scale isolation of antitumor agents from natural sources*

Deadline: *Approximately Aug. 31*

This procurement is totally set aside for small business. The size standard for small business is 500 employees or less.

NCI's Div. of Cancer Treatment will make available to interested contractors a request for proposals concerning a project to extract, isolate, and purify antitumor agents from plant and animal materials on a pilot plant scale. The contractor must provide a pilot plant facility capable of storing up to 50,000 lbs. and processing up to 20,000 lbs. of bulk crude material and must have experience in process development of natural products isolations.

The government will supply the plant and animal materials to be processed. The contractor will supply all equipment, solvents, reagents and other materials needed for the project. The antitumor agents isolated must be of high purity suitable for subsequent manufacture of clinical dosage forms and all work must be carried out under current Good Manufacturing Practices standards.

It is planned that one contract will be awarded for an incrementally funded three year period of performance. It is anticipated that a cost reimbursement type contract will be awarded requiring a level of approximately 5.5 staff years in year one, 4.0 staff years in year two, and 2.5 staff years in year three.

Contract Specialist: Ann Linkins
RCB, Blair Bldg. Rm. 220
301-427-8737

NCI CONTRACT AWARDS

Title: Cancer Control Program for clinical cooperative groups

Contractor: Cancer Therapy & Research Foundation of South Texas, $487,648.

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