THE CANCER LETTER

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RESPONSE FROM CENTER REPRESENTATIVES IN L.A. TO NCI QUESTIONS IS "FRUSTRATING," DEVITA SAYS

The President's Cancer Panel took its traveling probe of the Cancer Centers Program to Los Angeles this week; the first day, at least, of the day and a half meeting did not go well for most parties involved.

(Continued to page 2)

In Brief

ROBERT WEINBERG TO RECEIVE BRISTOL-MYERS AWARD; LEFFALL CHOSEN FOR POSTER SERIES

ROBERT WEINBERG, whose research group first demonstrated the existence of oncogenes in cancer caused by chemicals and other environmental influences, will receive the seventh annual Bristol-Myers Award for Distinguished Achievement in Cancer Research. Weinberg's group also was first to demonstrate that a single genetic change can transform a normal gene into a malignant oncogene. Weinberg was selected for the $50,000 award by an independent peer review committee chaired by Albert Owens, director of the Johns Hopkins Univ. Oncology Center.... **LASALLE LEFFALL,** chairman of the Dept. of Surgery at Howard Univ., has been selected by CIBA-GEIGY for its 1984 Exceptional Black Scientists Poster Series. The posters, distributed nationally to educational and community organizations, are made from a portrait by Ernest Crichlow. Leffall is a member of the National Cancer Advisory Board and a former president of the American Cancer Society.... **SUSAN BAIRD,** chief of cancer nursing at the NIH Clinical Center, will present the keynote address at the annual congress of the Oncology Nursing Society in Toronto. Her topic: "Communication, Cooperation, Collaboration—Cornerstones for Specialty Achievement." Eileen Depastino will present the annual Mara Mogensen Flaherty Memorial Lecture on the psychosocial aspects of cancer.... **ANIMAL RESEARCH** and testing will be the focus of a public policy forum May 7 in Washington DC, sponsored by the National Coalition for Science & Technology. Participants will look at trends in legislation and regulation and attempt to formulate appropriate responses. Contact Sklar, Idelson, 800 18th St. NW, Washington DC 20006, phone 202-223-8460.... **CHARLES DAHLE** will retire Sept. 30 as national director of media relations for the American Cancer Society. Dahle has been with ACS for more than 34 years, first in California and the last five in his present position.... **CONTRIBUTIONS** to the American Cancer Society set an alltime record of $203 million during the fiscal year which ended last Aug. 31. This was an increase of 11 percent over the previous year. Of that amount, 28.2 percent went for research, 26.8 percent for public and professional education, 19.8 percent for patient and community services, the rest for management and fund raising expenses.

STECKEL ASKS FULL FUNDING OF CENTERS, SEPARATE CANCER CONTROL CORE GRANTS

(Continued from page 1)

In the first place, the turnout at the Univ. of Southern California Comprehensive Cancer Center was disappointingly small considering that this was the only scheduled appearance of the Panel in Southern California for its hard look at centers which, conceivably, could lead to significant changes in the centers program. The audience consisted mostly of those making the presentations, NCI staff, and a few members of the USC faculty and staff.

Los Angeles Mayor Tom Bradley graciously welcomed the Panel with a brief but knowledgeable discussion of the two comprehensive cancer centers in his city and their activities. But he was the only public figure and the only representative of the lay community to address the Panel.

After the discussions Monday, NCI Director Vincent DeVita said he was "frustrated" by the responses evoked by a series of questions he had presented at the start of the meeting.

It has become clear after the first two of the current series of Panel meetings that DeVita is presenting tough questions. Center representatives will find themselves embarrassed if they are not prepared with some answers.

For example:

*DeVita referred to cancer mortality by sites in the 10 counties making up Southern California, noting several in which mortality exceeded the national average. Then, after hearing from the centers about the high number of oncologists practicing in the area, DeVita asked, "Why is your mortality from breast cancer higher than the national average, if you have all this expertise? Has anyone looked at areas where it is lower, to see what they are doing that you aren't? Do you have the mechanisms to find out why, with this concentration of medical expertise and sophisticated centers, your mortality from breast cancer is higher?"

"You can't compare different areas necessarily," Richard Steckel, director of the UCLA Jonsson Comprehensive Cancer Center said. Maybe we're catching them later."

"Shouldn't we know that?" DeVita persisted.

Steckel agreed and suggested that more support from NCI for clinical epidemiology and patterns of care studies would help.

Brian Henderson, director of the USC Comprehensive Cancer Center, argued that the county by county mortality rates "go back a quarter of a century, and we do not have the cancer incidence data in the 10 counties... The incidence of breast cancer in Los Angeles County is quite high, among the highest in the United States, in fact the world. I'm not sure that the conclusion that case mortality is higher is correct."

DeVita agreed with that possibility but insisted that centers should look at mortality data in their regions for clues on studies they should be emphasizing.

*DeVita said that "In my meandering around Southern California, I've been told that you do not get the referrals you should be getting at centers. There are only 1,200 patients on protocol in the area, out of 52,000 new patients a year. That indicates that most of the patients here are not benefitting from state of the art treatment. You do have a problem with community physicians."

John Hisserich, deputy director of the USC center, said, "This is an extremely rich area in oncology resources. Many community physicians are reluctant to refer patients for the kinds of protocols we have at centers. They may be more aggressive than the community physicians are comfortable with. We have not been particularly successful in working with community physicians."

James Doroshow, director of medical oncology and therapeutic research at the City of Hope National Medical Center, said that "hundreds of physicians refer patients to City of Hope. But, you have to have something innovative, something special to offer, or you don't get referrals. There are thousands of patients in the Los Angeles area who are appropriate for clinical trials who are not going into protocols."

DeVita said that the Panel and a planning committee of the Div. of Cancer Prevention & Control are looking at such issues as:

—What are the special problems and opportunities in the population groups in the region?

—What programs do centers have to address these special problems in the region?

—What are the unique features and accomplishments of each center?

—Are the relationships between each center and the components of the NCI network, such as CCOPs, cooperative groups, other NCI grantee institutions and practicing oncologists functioning well?

—What are the relationships between each center and other organizations and institutions with a role in cancer control?

—What opportunities exist for exploiting the training potential of centers, especially for minority students and scientists?

—How do we know when a region needs additional centers? Are more or different kinds of centers required for Southern California?

—What new control activities could centers initiate?

--If these activities are not seen as the responsibility or mission of centers, whose respons-

bility are they?

Also, "How many centers are needed. What is the proper mix of centers? Consortium centers are a concern. They have some difficulties, which we hope can be corrected."

And finally, "How should we support basic research centers? Are basic centers losing support?"

On that last point, DeVita has suggested for the past two years that centers involved only in basic research might do better with a mechanism of support better than the core grant—probably the program project. Program projects (PO1s) and RO1s are always protected in the NIH budget manipulations. The dollar pool supporting them is the last to be cut, and when Congress last year ordered that NIH research grants be funded at their full peer review recommended levels, NIH decreed this would apply only to RO1s and PO1s. Cancer center core grants were funded at only 85 percent of the recommended levels. All grants, including RO1s and PO1s, will be cut this year under the President's budget, although Congress may change that again.

DeVita's point is that a basic research cancer center now with a core grant could do better if that were to be switched to a program project. However, he has not had much luck in selling that view. The DCPC Board of Scientific Counselors rejected the suggestion two years ago, and the response from basic science center representatives at the Birmingham and Los Angeles meetings of the President's Cancer Panel was cool.

DeVita also asked whether a clinical link should be required for basic science centers. "If so, how can collaborative efforts between basic and clinical research activities best be encouraged? What is the relationship of each basic science center to clinical and comprehensive centers in the region?"

Panel Chairman Armand Hammer, Panel members William Longmire and John Montgomery, DeVita and NCI staff members have tried to encourage center and community representatives to discuss the particular problems and needs of their areas, their plans for meeting those needs, and the resources they will require for carrying out those plans. A few of those making presentations have responded along those lines at the two meetings so far, but most have missed the mark, preferring to discuss research being carried out in their institutions or merely describing the organizational makeup of their centers.

No one so far has seized the opportunity for a coordinated presentation, using political, business, and lay community leaders to attempt to sell the Panel and NCI on supporting new, creative programs to address local cancer problems.

Steckel did use some of his time to make a pitch for increased funding of core grants. He offered four specific recommendations which he said "in my opinion would help to ensure the present and future effectivenmess of cancer centers receiving NCI support." They were:

"1. Steps should be taken to ensure that approved core grants for cancer centers are funded at budget levels which are at (or close to) the levels which have been recommended by peer review. At present, core grants are being funded at 85 percent of recommended budget levels, recommended levels which have already been reduced substantially during the peer review process. Since core grants are directly supportive of RO1 and PO1 investigators at centers, it is as important to fund core grants at recommended levels as it is to fund the individual research projects which they are targeted to support.

"2. While considerable improvements have already been made, it is essential that the quality of NCI reviews of core grants be improved further with the use of consultant reviewers of the highest quality and experience.

"3. Core grants designed specifically for cancer control research should be made available to centers, and should be based upon the quality and the 'centeredness' of cancer control research at the applicant institution. The present small supplements (for cancer control research) to existing cancer center core grants are welcome, but they are not adequate. At the present time, only two individuals can be supported through these supplemental grants. More adequate cancer control core grants for centers, which are designed specifically to provide administrative and logistical support for peer reviewed and funded RO1 and PO1 cancer control research projects, will become increasingly necessary as cancer control research comes into its own at centers.

"4. There is a backlog of unmet needs for renovation and construction of research facilities at cancer centers, including the growing realm of cancer control research. This backlog should be met through the renewed availability of NCI construction and renovation funds, to be matched by substantial funding from local and institutional sources."

Lester Breslow, dean emeritus of the UCLA School of Public Health and chairman of the DCPC Board of Scientific Counselors, suggested six specific functions as the role of centers in cancer control:

1. With NCI, each center should define the geographical area it serves "as an NCI outpost."

2. In cooperation with state and local agencies, centers should analyze and publicize the nature of the problems in their regions.

3. Centers should set objectives for cancer control in their regions along the lines of NCI's national objectives (e.g., reduce mortality by 50

percent by the year 2000, with specific programs aimed at certain cancer sites, exposures, etc.).

4. Centers should monitor and report trends in cancer phenomena and patterns of care, survival, prevention efforts.

5. Centers should provide technology assessment to all appropriate agencies on prevention, diagnosis, treatment, rehabilitation and continuing care.

6. Centers should provide the central effort in their regions for cancer control and should conduct cancer control research.

Breslow said that while the 1970s has been called the "decade of discovery, the 1980s and 1990s will be the decades of cancer control."

For the record, here are the cancer mortality rates in Southern California counties which exceed the national rates, as reported by DeVita at the Panel meeting (extracted from SEER data, for whites):

Breast cancer—Los Angeles County, 31.4; Santa Barbara County, 32.6. U.S. rate, 28.2.

Ovarian cancer—Los Angeles, 9.8; U.S., 8.8.

Buccal cavity and pharynx—Los Angeles, 4.3; U.S., 3.6.

Lung cancer—Kern County, 49.6; San Diego County, 46.4. U.S., 42.6.

Cervical cancer—Kern County, 5.9; U.S., 3.6.

Henderson in his presentation reported on several epidemiological studies in the region, including one not yet published which could offer an important new insight into the etiology of colon cancer.

The study, headed by David Garabrant, found that persons engaged in sedentary occupations, as opposed to those in occupations with moderate or high degree of physical activity, have higher rates of colon cancer. "The colon cancer rate goes down remarkably, with a two fold difference, as the activity rate goes up," Henderson said.

That study looked only at occupations. A new study just funded will attempt to assess the effect of all types of physical activity, for instance, if running, swimming, etc. by persons in sedentary occupations reduces colon cancer risk.

A study of local Chinese populations essentially confirmed earlier reports that consumption of a certain type of salted fish produces as much as a 30 fold increase in the risk of nasopharyngeal cancer if eaten weekly. "This is the first food directly linked to the cause of a human cancer," Henderson said.

A mesothelioma study found that, "To our surprise, much of the increase in the incidence was an artifact of reporting. There has been little, if any, increase." Henderson later explained that physicians, after detecting what really was lung cancer, assumed it was mesothelioma after learning that the patient had worked in a shipyard or had been otherwise exposed to asbestos.

A lung cancer study by census tract found no evidence that persons living in areas with high degrees of air pollution are at higher risk for the disease. "It's not a question of where you live, but where you work and how much you smoke," Henderson said. "It is hard to measure in the face of cigarette smoking." Henderson added that there is no evidence of synergism between cigarette smoking and air pollution.

A study headed by Tom Mack of persons living near dump sites so far has found no evidence that those dumps affect the distribution of cancer incidence.

In a study of residents of a Southern California retirement community, with 364 cancers reported, there was no difference in cancer incidence for those using vitamin A supplements compared with those who do not.

One of the tougher, potentially embarrassing, and perhaps unfair questions asked by NCI was that by Jerome Yates, director of DCPC's Centers & Community Oncology Program.

Yates directed the question to Hisserich and Steckel. Noting that the Community Based Cancer Control Program, one of NCI's largest and most controversial cancer control efforts of the 1970s, included a large contract in Los Angeles, Yates asked, "What happened after that? What planning and permanent activities came out of it?"

Steckel responded that one part of the CBCCP effort still going is a program to teach breast self examination, and that several institutions are continuing various psychosocial programs.

Hisserich said, "We learned how to approach community groups. We brought in a lot of organizations not previously active in cancer control."

Those answers obviously were not adequate, considering that CBCCP was a five year program, averaging about a million dollars a year for each of the contractors. However, there were others more involved in the Los Angeles programs than Steckel and Hisserich who might have provided a more complete picture of the effects it had on cancer control in L.A. and of what elements are still in operation. In fact, an analysis of the entire program and all the contractors involved would be interesting and might be useful.

EPIDEMIOLOGIST SAYS STUDIES LINK CERVICAL CANCER, CIGARETTE SMOKING

A Univ. of California epidemiologist last week summarized the results of six studies which show an association between cigarette smoking and cervical cancer, with one of the studies finding that women

who smoke are 17 times more likely to develop carcinoma of the uterine cervix than were nonsmoking women.

Warren Winkelstein, professor of epidemiology at UC (Berkeley), discussed his hypothesis on the association of smoking and cervical cancer at the annual American Cancer Society Science Writers Seminar. He said that data from the Third National Cancer Survey revealed a high geographical correlation between the incidence of cancer of the trachea bronchus and lung in males and cancer of the uterine cervix in females.

Winkelstein and his colleagues concluded that cancers which varied together in the nine communities of the TNCS might have common environmental causal factors. Second, it had long been known that smoking-related cancers are predominantly, although not exclusively, characterized by a certain dominant cell type, squamous epithelial cells. Since both cervical cancer and lung cancer are predominantly made up of these cells, and since they varied together geographically, it was hypothesized that they might have a common cause. The causal relationship between cigarette smoking and lung cancer has been well established for close to a quarter of a century.

At the time the hypothesis was proposed, five studies had been carried out in which relevant data had been reported. In all but one of these studies, an association was demonstrated. However, in none had the investigators been able to adequately deal with the possibility that the smoking assocation might have been due to an underlying association between smoking and sexual promiscuity, long known to be the most important risk factor for cervical cancer. Nor had these investigators recognized that the association might have causal implications.

In the six studies which have been reported since publication of the hypothesis, the study designs have made it possible to control for this possible confounding. All six have revealed independent associations between numbers of sexual partners and smoking with cervical dysplasia and carcinoma in situ. Nevertheless, several of the inestigators involved have been skeptical of their own findings. One discounted the observation on the basis that the smoking habit might have reflected some important aspect of sexual behavior over and above those which were measured, namely, age at first intercourse and number of sexual partners. Another discounted the association on the basis that it was not biologically plausible.

Both of these possibilities have been examined by Winkelstein and his colleagues and their conclusions published in the January issue of the "American Journal of Epidemiology." They contend that the possibility that the association is due to an unknown "confounding sexual practice" would require that the practice be very common, in fact, having a prevalence in the general population of at least 50 percent as well as being 3 1/2 times as prevalent as smoking and having a relative risk of producing dysplasia or cervical cancer of 3 1/2. The likelihood that such an unknown sexual practice has been overlooked in studies of the causation of this disease seems most unlikely.

As far as biological plausibility is concerned, Winkelstein cited evidence for the association of squamous cell cancers and smoking, for the repeated demonstration that carcinogenic chemicals introduced into the body by a variety of entry modalities can be circulated to distant organ sites where cancers have developed, and for the observation that cancers for which causative agents have been established are frequently subject to multiple causation. Additionally, they have suggested that the demonstration that sexual promiscuity as well as cigarette smoking are independently associated with cervical cancer indicates the possibility that both a viral and chemical carcinogenic agent may produce the disease. They point to little known research conducted in the 1930s which indicated that in animals, chemical carcinogens could potentiate the effects of tumor producing viruses.

Winkelstein said recent observations show that the association of smoking and cervical cancer was strongest in young women. In fact, in a study conducted by investigators at the Univ. of Utah, the relative risk for smoking women vs. nonsmoking women under the age of 30 was 17. Stated another way, smoking women were 17 times more likely to develop carcinoma in situ of the uterine cervix than were nonsmoking women independent of their sexual experience.

Cancer of the uterine cervix is the fifth most common cancer of women. Lung cancer and cervical cancer combined are exceeded only by breast cancer. Thus, a substantial proportion of cancer in females would now apparently be preventable if the common practice of smoking cigarettes could be curtailed, Winkelstein said.

Saul Gusberg, former ACS president and a gynecologist, noted that the increase in cigarette smoking among women in general has been paralleled by an increase in the incidence of in situ carcinoma of the cervix. "It is a paradox. While invasive cancer of the cervix has gone down steadily since the widespread use of the Pap test, in situ cervical cancer has gone straight up."

Regina Ziegler, with NCI's Environmental Epidemiology Branch, described two recent NCI case control studies which demonstrated that improvements in nutrition can reduce the risk of esophgeal, oral, and pharyngeal cancer.

One study was of esophageal cancer among black males in Washington D.C. Esophageal cancer is unusually high among urban black males, and Washington is the U.S. metropolitan area with the highest esophgeal cancer mortality rate for this population. The next of kin of 120 esophageal cancer cases and 250 controls were interviewed. Alcoholic beverage consumption was the predominant risk factor, with the risk of esophageal cancer among drinkers being six times that among nondrinkers. However, general nutritional status was also a risk factor, whether measured by consumption of fresh and frozen (not processed) meat and fish or by diary products and eggs or by fruit and vegetables, or even by the number of meals eaten per day.

the least nourished third of the study population, defined by any of these measures, had twice the risk of the most nourished third. When the extremes were compared, the men who consumed low levels of fresh and frozen meat and fish, and low levels of dairy products and eggs, and low levels of fruits and vegetables versus the men who consumed high levels of all three food groups, the relative risk reached 14 in the low consumers. Nutritionally neutral food groups, such as bread and carbohydrates, were not associated with risk.

The association between esophageal cancer and diet was shown not to be simply the result of a correlation between poor diet and heavy drinking. In fact, both light drinkers and heavy drinkers seemed to have comparable reductions in risk with improved diets. There were too few nondrinkers in the study population to assess the impact of improved diet on their risk.

The assocation between esophageal cancer and diet was also shown not to be a result of smoking nor of other lifestyles correlated with socioeconomic status. Estimates of the intake of several vitamins, specifically, vitamin A, carotene, vitamin C, thiamin, and riboflavin, were calculated and were lower in the cases than in the controls. But these estimates of vitamin intake were less persuasively associated with risk than were broad food groups, such as fruits and vegetables. Thus no specific vitamin deficiency was identified. Generally poor nutrition, along with heavy alcohol consumption, seemed to be the best explanation of the susceptibility of urban black men to esophageal cancer.

The second case-control study was of oral and pharyngeal cancer among women in North Carolina. Mortality rates for these two cancers are unusually high among white women in the Southeast U.S. For the study 227 cases and 405 controls, or their next of kin, were interviewed. Snuff dipping and cigarette smoking were the predominant risk factors, with risk among the white women who dipped or smoked or did both being three-four times that among women who did neither. Fruit and vegetable intake showed a protective effect, with women in the lowest quartile of fruit and vegetable consumption having twice the risk of those in the highest quartile, after controlling for tobacco habits. Moreover, among the low fruit and vegetable consumers, dipping and smoking had the most effect. This relationship of diet to oral and pharyngeal cancer was shown not to be an indirect result of alcohol use, dental health, or socioeconomic status.

Although these two case-control studies focused on different cancers—cancer of the esophagus and of the oral cavity and pharynx, a number of similarities exist in the dietary relationships uncovered.

1. In each study eating more of certain food groups was found to be protective, to reduce the risk of cancer. All too often people assume fatalistically that everything they eat has the potential to cause cancer, and they forget that certain dietary patterns actually seem to reduce cancer risk.

2. In each study the dietary patterns associated with a noticeably reduced risk of cancer were characteristic of a quarter or third of the people in the study, and the people selected for the study were representative of those living thoughout the state or region. Thus no drastic changes in diet had been adopted to reduce risk by the 50 percent noted in these studies. For example, in the esophageal cancer study the men who had the 50 percent reduction in risk ate three or more servings of fruit, vegetables, or juice daily. In the oral-pharyngeal cancer study the women with the 50 percent reduction in risk ate three or more servings of fruit or vegetables daily. These are not impossible goals.

3. The dietary patterns that substantially reduced risk in these studies did not require the use of high dosage food or vitamin supplements. A moderate increase in consumption of certain common food groups was all that was necessary.

4. Neither of the studies identified as a risk factor low intake of a specific vitamin. In the esophageal cancer study food group consumption was more predictive of risk than calculated vitamin intake. Whereas the risks associated with low fruit and vegetable consumption, low meat and fish consumption, and low dairy and egg consumption were of the order of two, the risks associated with low intake of vitamin A, carotene, riboflavin, and thiamin were about 1.5. Thus the biological mechanisms whereby these food groups reduce cancer risk were not clarified. For example, fruit and

vegetables could be important because of their content of vitamin C, carotene, fiber, trace minerals, indoles, or something else, or a combination of any of these. But from a public health perspective, it is irrelevant. Increased consumption of certain food groups, whatever the mechanism, was associated with decreased risk.

5. For both of these cancers more than one risk factor was identified. Alcohol or tobacco or snuff increased risk; in the same individuals diet decreased risk. However, although diet was capable of reducing the risk attributable to these other exposures, it could not totally eliminate it. For example, in the esophageal cancer study a wholesome diet decreased the risk associated with alcohol consumption in both light and heavy drinkers, but alcohol remained a potent risk factor, with the risk of esophageal cancer still proportional to its intake.

In one significant way, however, the two case-control studies are not alike. Somewhat different, albeit compatible, dietary patterns, were associated with reduced risk. Generally poor nutrition increased the risk of esophageal cancer; while low fruit and vegetable intake increased the risk of oral and pharyngeal cancers. The relationship of diet to cancer may well vary for different sites.

Tracy Wilkins, professor of microbiology at Virginia Polytechnic Institute, suggested that colonic bacteria may produce carcinogens which cause colon cancer and that it may be possible to intervene in that process.

Colon cancer is an environmental disease that is caused in some manner by a highly refined and high fat diet. In countries where the population cannot afford to remove the husks from their grains (bran) and where oils and fats are used sparingly, this disease is very uncommon. We do not know how diet acts to result finally in colonic carcinoma, but the entire diet seems to be at fault; no single ingredient can be incriminated.

The colon has a very large surface area that is exposed to the outside environment, which, in this case, consists of one of the highest and most diverse concentrations of anaerobic bacteria on earth. There are over 400 species of bacteria in our colons and these metabolic factories could be producing carcinogenic waste. We have shown that in the colons of affluent populations these bacteria produce a mutagenic compound that could cause alterations in the DNA of the colonic cells. Almost all carcinogens are mutagens, but not all mutagens are carcinogens. The problem is to determine which mutagens are a danger to humans.

The compound turned out to be a previously unknown type of molecule. This class of mutagenic ether-lipids has now been given a name, fecapentaenes. David Kingston in the Chemistry Dept. at VPI has synthesized fecapentaenes for the first time, and shortly will have enough of these compounds to begin carcinogenicity tests in animals.

The fecapentaenes are responsible for the majority of the mutagenic (DNA damaging) activity in the human colon. Much higher concentrations were found in samples from North Americans than in samples from rural blacks in South Africa (who have a very low rate of colon cancer). Fecapentaenes are produced by some of the most common bacteria in the human colon, but the conditions must be just right before production occurs.

Synthesis of the fecapentaenes is dependent first on the presence of another compound in the colon which was termed precursor-X. No one yet knows where this compound comes from or what it is. A second condition for production is the need for bile. North Americans secrete larger amounts of bile than populations that eat lower fat diets, so there is enough bile in our colons for the bacteria to complete the synthesis. Fiber also could be important because the consumption of fiber would dilute the bile and precursor as well as prevent the synthesis in other ways. Thus when the bacterial factories are fed a low fat, high fiber regimen their effluent may not be as mutagenic as when they are given richer food.

This is only one of many areas being investigated in a concerted effort to find the causes of human colonic cancer. There may be many ways in which colon cancer can be initiated, and it is unlikely that there will be a single simple solution to preventing the disease. Massive changes in diet are unlikely to be accepted by the majority of people even though such a change could reduce the incidence of this disease, Wilkins said. Other means of prevention must be found. If some colon cancers are caused by the accumulation of carcinogenic bacterial products this could be thought of as an unusual bacterial disease that may be preventable like most other bacterial diseases.

The view that Americans are unlikely to make significant changes in their diet when motivated by health reasons is not shared by NCI or the American Cancer Society. Both have initiated nationwide public education efforts to encourage reduction of dietary fat and increase of fiber and vitamin A/beta carotene containing foods. Wilkins agreed that those efforts are worthwhile and that some important modifications could be achieved.

Wilkins' colleagues in the study were Roger VanTassell, David Kingston, and Leslie Gunatilaka of VPI, and Bob Bruce of the Ludwig Foundation for Cancer Research in Toronto.the Ludwig Foundation for

RFA NIH-NCI-DCPC-CCAB-CA-07
Title: Cancer control small grants research program
Application receipt date: May 15

The Div. of Cancer Prevention & Control of NCI invites small grants research applications from interested investigators. This program is designed to aid and facilitate the growth of a nationwide cohort of scientists with high level of scientific research expertise in the field of cancer control. Its major objective is to encourage new investigators from a variety of academic disciplines to apply their skills to scientific research in the field of cancer control intervention research. The intent is to fund up to 10 awards with total costs for all projects amounting to $350,000. This level of activity is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of NCI, the award of grants pursuant to this RFA is also contingent upon the continuing availability of funds for this purpose.

Cancer control is defined as the reduction of cancer incidence, morbidity, and mortality through an orderly sequence from research on interventions and their impact in defined populations to the broad, systematic application of the research results. Cancer control research studies are classified into one of five phases which represent the orderly progression noted in the above definition: (1) hypothesis development; (2) methods development and testing; (3) controlled intervention trials to establish cause and effect relationships; (4) research in defined populations; and (5) demonstration and implementation studies. DCP C is primarily interested in research on cancer control intervention in phases 2 through 5.

Allowable direct costs include personnel, supplies, publication costs, travel, and equipment expenses. In general, total costs (direct and indirect) should not exceed $35,000. The duration of support is one year but may be longer (up to two years) if the funding limits noted above are not exceeded.

Grants may be awarded to profit and nonprofit organizations and institutions, governments and their agencies, and occasionally to individuals.

Investigators are eligible to apply for a small grant to support research on a cancer control topic if they have never received NCI cancer control funding and are interested in conducting exploratory studies in cancer control research.

Submission of an application under this announcement precludes concurrent submission of a regular research grant application containing the same research proposal. In addition, small grant research support may not be used to supplement research projects currently supported by federal nor nonfederal funds, or to provide interim support of projects under review by the Public Health Service.

Responsive applications will be reviewed for scientific and technical merit by a committee consisting primarily of nonfederal technical and scientific experts and will be evaluated subject to the following criteria:

1. Quality of the principal investigator's education and/or scientific training, and potential for contribution as an investigator in the field of cancer control intervention research.
2. Evaluation of the research proposal for scientific merit, including originality, feasibility, adequacy of design, plans for analyses and evaluation of data, and soundness of the research plan.
3. Adequacy of resources and the supportive nature of the research environment.
4. Appropriateness of the proposed budget.
5. Significance in relation to cancer control intervention research.

Unresponsive applications, i.e., those not meeting the criteria for cancer control intervention research, will be returned.

The regular research grant application, form PHS-398, must be used in applying for these grants. These forms are available at most institutional business offices; from the NIH Div. of Research Grants, Bethesda, Md. 20205; or from the program director (see below).

These grants will be reviewed in July with the earliest possible funding date in September.

Certain limitations in addition to usual NIH requirements apply in the writing of these applications. Biographical sketches may not exceed one page; specific aims and signifiance, one page each; progress report and preliminary studies, if applicable, two pages; experimental design and methods, 10 pages; and human subjects and literature cited, two pages each. These limitations and others in the PHS-398 application instructions must be observed or the application will not be accepted.

For program information, contact Dr. Robert Burnight, Program Director, Career Development Unit, Cancer Control Applications Branch, DCP C, NCI, Blair Bldg Rm 1A09, Bethesda, Md. 20205, phone 301-427-8788.

For grants administration information, contact William Wells, Grants Management Specialist, Grants Administration Branch, NCI, Westwood Bldg Rm 855, Bethesda, Md. 20205, phone 301-496-7800.

RFP EXTENSION
RFP NCI-CP-EB-41026-60
Title: Investigations of cervical cancer in Latin America

The deadline for receipt of proposals for this RFP, availability of which was published in the March 9 issue of **The Cancer Letter**, has been extended from May 14 to May 30.

The Cancer Letter _Editor Jerry D. Boyd

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