

THE

# CANCER LETTER

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## Michael Grever To Head DTP; Chabner's Deputy Is Kaufman; Radiation Program To Be Split

Bruce Chabner, director of NCI's Div. of Cancer Treatment, has made considerable progress toward filling vacancies created by the impending departure of senior staff members: **Michael Grever**, who has been DCT deputy director for the past two years, and who has also served as acting associate director and head of the Developmental Therapeutics Program (Continued to page 2)

### In Brief

## Univ. Of Pittsburgh Creates Genetics Institute; Elion Inducted Into Inventors Hall Of Fame

UNIV. OF PITTSBURGH has created the Pittsburgh Genetics Institute, a federation of scientists and clinicians working on genetics research and treatment. **John Mulvihill**, chairman of human genetics at Pitt's Graduate School of public health and formerly of NCI, and **Joseph Glorioso**, Pittsburgh School of Medicine, are co-directors of the institute. PGI will receive \$1.5 million in start-up funds from UPMC for faculty recruitment and research costs. . . . **GERTRUDE ELION**, scientist emeritus at Burroughs Wellcome and past member of the National Cancer Advisory Board, is one of eight inventors elected to the National Inventors Hall of Fame this year. She is the first woman inventor to be inducted. She was elected for patenting drugs crucial to the treatment of cancer. . . . **DAVID GOLDENBERG**, president and founder of the Center for Molecular Medicine and Immunology in Newark, NJ, was awarded the 1991 3M Mayneord Memorial Prize and Lectureship by the British Institute of Radiology. . . . **HAROLD MOSES**, chairman of the Dept. of Cell Biology at Vanderbilt Univ. School of Medicine and a member of the Div. of Cancer Biology, Diagnosis & Centers Board of Scientific Counselors, has received the Rous Whipple Award from the American Assn. of Pathologists. . . . **SYMPOSIUM ON MINORITIES**, the Economically Disadvantaged & Cancer is scheduled for April 17-20, in Houston, TX. Contact Dr. Lovell Jones, Dept. of Gynecology, M.D. Anderson Cancer Center, phone 713/792-3316, fax 713/792-7586. . . . **JOSHUA ATIBA** has joined the Univ. of California (Irvine) Clinical Cancer Center as assistant professor of medicine and pharmacology, Div. of Hematology/Oncology. Atiba was chief resident at Vancouver General Hospital. . . . **ALEXANDRA LEVINE** has been named chief of the hematology division in the Univ. of Southern California School of Medicine. She succeeds Donald Feinstein, who resigned the post after being named chairman of the medicine department at the new University Hospital. Levine will continue as deputy director of the Kenneth Norris Jr. Cancer Hospital.

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## Grever To Head DTP, Chabner's New Deputy Is Kaufman; RRP To Be Split

(Continued from page 1)

for more than a year, will give up the deputy position and become permanent director of DTP.

Grever had been a major figure in drug development at Ohio State Univ. before joining NCI; when Michael Boyd decided to relinquish the DTP director's job and go back into hands on research as chief of the new Laboratory of Drug Discovery Research & Development, Grever decided to compete for the job and won it.

**Dwight Kaufman** has been named by Chabner as the new DCT deputy director. Kaufman, an MD and PhD, has been a senior investigator in the Medicine Branch of DCT's Clinical Oncology Program and also holds an appointment in the Radiation Research Program.

**Bruce Johnson**, senior investigator in the NCI-Navy Medical Oncology Branch, became acting chief of that branch when its chief, John Minna, left this week for his new job as director of the Howard Simmons Cancer Center in Dallas. Minna had recommended Johnson for the acting job and suggested he would be a serious contender for the permanent appointment. Chabner agreed, although pointing out that the position would be filled through open competition.

**Ruth Ann Giusti**, a third year fellow in the Clinical Oncology Program, will become Chabner's special assistant for clinical affairs when Mace Rothenberg leaves this summer for his new job with the Southwest Oncology Group and the Univ. of Texas Health Science Center in San Antonio. An epidemiologist, Giusti has been with the Centers for Disease Control and has been working with William Blattner of the

Environmental Epidemiology Branch in the Div. of Cancer Etiology.

### Radiation Program Shakeup

Chabner is planning a major shakeup in the Radiation Research Program in the wake of the departure of **John Antoine**, who headed that program for the last five years. Antoine has joined the intramural program's Radiation Oncology Branch as a senior investigator.

**Michael Friedman**, associate director and head of the Cancer Therapy Evaluation Program, has been acting director of RRP.

RRP supports extramural research in both imaging and radiation therapy. Chabner has discovered that it is very difficult to find people with expertise in both of those areas, who also possess the leadership qualities the job requires, and who are willing to come to NCI.

The Div. of Cancer Treatment Board of Scientific Counselors has approved Chabner's suggestion that RRP be divided into two programs, imaging and radiation therapy, each with its own associate director reporting directly to him.

"It's still possible we could find someone who could do both, and if we do, we won't split it up," Chabner told **The Cancer Letter**. However, he is going ahead with interviews on the assumption that there will be two programs.

## New CCOP Lineup Remains Unclear, Research Bases Especially; 11 Ok'd

The new lineup in the Community Clinical Oncology Program, for the CCOPs and their research bases, remains unclear as the June 1 deadline for completion of the awards gets closer.

All of the research bases had to recompute their cooperative agreements last year. Despite the fact that review was completed last November, and submission to the National Cancer Advisory Board was made in February, the total number that will be funded has not yet been determined.

The problem is that the number of CCOPs which will be funded in the just completed round is still uncertain. NCI's Div. of Cancer Prevention & Control had intended to fund from three to five in this round, depending on how much money is available.

That can't be determined until the continuation applications of the noncompeting CCOPs, which includes most of them, have been reviewed and their new annual budgets approved. Those applications were due April 1.

Unlike most NIH grants, the CCOP cooperative

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agreement budgets are not predetermined for the length of the award but are adjusted each year, depending on performance. Thus, reductions from the anticipated continuation awards could make more money available to fund competing awards.

This leaves the research bases up in the air, for the moment. There have been 14 organizations serving as research bases for the program; 15 applications were submitted in the recompetition. Four of those were disapproved, which would seem to indicate that all 11 of the approved submissions could be funded.

That might happen, but not necessarily. A research base must have a viable number of performing, affiliated CCOPs to be funded. Some of the research base applicants may be dependent on CCOPs involved in the recent competition for that "viable" number.

Priority scores were assigned to the research base applications, but awards will not be based on them.

**Progress on evaluation** of the program, carried out by the Univ. of Illinois under a contract with DCPC, was reported at the annual meeting of the Assn. of Community Cancer Centers by Richard Warnecke, director of the university's Survey Research Laboratory.

Warnecke said the evaluation has four objectives:

1. "Look at implementation, how the group is organized, how the organization has moved toward accrual, relationships with research bases and among the CCOP components."

2. "Describe and characterize the roles of DCPC and the Div. of Cancer Treatment in the process."

3. "Look at the impact of the CCOP on the community. This includes practice patterns, a diffusion study" [Warnecke pointed out that the previous evaluation of CCOP did not look at changes in practice]. This time, the impact of CCOPs on three major sites will be analyzed--stage 2 breast cancer, some aspects of stage 1 breast cancer, and any changes in colon cancer. Our hypothesis is that, if a CCOP is having an effect, we should see improvement in patients not treated by CCOPs."

4. "Changes in the research agenda. How the CCOP has become institutionalized. Has it become part of the cancer program of the hospital? Has the CCOP become a permanent component of the institution?"

The evaluation, of course is also considering the impact of CCOPs on accrual of patients to clinical trials.

Albert Einstein, medical director of the Virginia Mason Medical Center in Seattle and principal investigator for that center's CCOP, chaired the ACCC session on the program. He reviewed the development of the program, noting that one of its goals was to

"increase accrual to clinical trials by getting the people involved who see most of the patients."

The program has worked very well, Einstein said. His CCOP is affiliated with the Southwest Oncology Group, to which CCOP patient entries "are very significant. We are full participants in the group, we have felt welcome. CCOPs have handled data management very well; Chuck Coltman (SWOG chairman) has said we do it better than the academic members.

"We're still learning to do cancer control, as the entire scientific community is still learning," Einstein said.

## **Studies Add To Information On Diet; Microwaved Meat Is Safer--Adamson**

Recent studies on the relationship between diet and cancer support the theory that a diet high in animal protein and fat and low in dietary fiber is a risk factor for certain cancers.

As much as one third of cancer incidence in the U.S. may be related to the Western-style diet high in animal fats and low in fiber, according to experts at an American Cancer Society meeting in Phoenix last week.

"These are very important leads," said Peter Greenwald, director of NCI's Div. of Cancer Prevention & Control. "The value in each of these papers is that [the researchers] have done a series of studies that seem to put information together."

Together, the message of the new studies is to reduce meat consumption, use low fat and low temperature cooking methods, and increase consumption of fiber, Greenwald said. In addition, a study by a New York Univ. researcher proposed several natural products, including green tea, as chemopreventive agents.

Greenwald said NCI is considering simplifying its dietary guidelines to resemble California's "Five a Day" program, which urges Californians to eat five portions of fruits or vegetables a day.

### **Protein And Cancer**

For the past 20 years, Colin Campbell, professor of nutritional biochemistry at Cornell Univ., has studied aflatoxin B, which was believed to induce hepatocellular carcinoma in rats. Studies in rats and humans over this period "now appear to show remarkable consistency and may illustrate much broader principles concerning the generic relationship between diet, nutrition, and cancer," Campbell wrote in his paper, "Dietary Protein and Liver Cancer: A

Model for the Study of Nutrition and Chemical Carcinogens," presented at the ACS Science Writers Seminar.

Campbell's research stemmed from the observation that among Philippine children, the children who grew the fastest had a greater risk of liver cancer. Campbell hypothesized that protein may help aflatoxin B (AFB) cause cancer. Based on further studies, Campbell now believes that protein alone, not AFB, is the important risk factor.

Campbell's most recent work is a geographic correlation study of 48 counties in China. The greatest risk factors for liver cancer in the China study were persistent infection with hepatitis B virus, elevated plasma cholesterol levels, and liquor intake.

"Even though aflatoxin intake varied widely, no relationship of aflatoxin intake with liver cancer was observed," Campbell wrote. "I consider rather remarkable the association of liver cancer with plasma cholesterol, which was associated in turn with a relatively small intake of animal foods. What is particularly impressive about these findings is the consistency observed between the human and experimental animal studies."

Campbell summarized the main hypotheses of this work and argued that these hypotheses on dietary protein probably apply to all cancers, "albiet to varying degrees for different individuals.":

1. Only small amounts of animal protein intake enhance tumor development.
2. A switch from animal protein to plant protein inhibits and may even reverse further tumor development.
3. The amount of dietary protein recommended for optimization of health is that which is provided by a diet comprised of a variety of plant foods. This amount of protein is approximatley 8 to 10 percent of the total weight of food eaten or an amount equivalent to the current RDA: 56 g/day for adult men, 48 g/day for adult women.
4. A diet comprised of plant protein permits a greater consumption of calories which does not increase tumor development.
5. Aflatoxin carcinogenicity for humans is unlikely to be as significant as once thought.
6. The most important dietary risk factor common to all cancers is the intake of animal foods, which include not only the animal protein but also a variety of other nutrient displacements favorable to cancer development.

Campbell was asked whether he would recommend that a person with hepatitis B infection become a vegetarian. "Yes, I take that very seriously," he said,

noting that his daughter became infected while working overseas in the Peace Corps, and now eats no meat. Campbell said he, too, is "very close" to being a vegetarian. The RDA level for protein can be acheived with a plant diet, he said.

However, Campbell said that while he is convinced that diet is a major factor in cancer, he supports further study, such as NCI's proposed Women's Health Trial, an intervention trial in women to show the effect of a reduction in dietary fat on incidence of cancer and heart disease.

"I've always been enthusiastic about that approach," he told *The Cancer Letter*. "I think this is essential. How else can we get definitive data?" The Women's Health Trial is "only the tip of the iceberg" in diet and nutrition studies that should be done, Campbell said. One concern with WHT is that the control group's level of dietary fat may drift downward over time, but Campbell said he doubts the diet of most Americans has changed to such a degree in recent years.

#### Diet And Hormones

Herman Adlercreutz, chief physician in the Central Laboratory, Helsinki Univ. Central Hospital, has compared the intake of dietary macro and micronutrients with plasma, urine, or fecal hormone levels in groups of women consuming different diets and in women who had been treated surgically for stage 1 or 2 breast cancer.

About 200 women in Boston, Hawaii, Japan, and Finland participated. The women were breast cancer patients, women eating a regular "Western-type" diet, or lacto-ovo vegetarians. Dietary records were obtained from participants, and a large number of hormones, lignans, and isoflavonoids were determined in plasma, urine, and feces. Adlercreutz also has done less extensive studies of the dietary effects of hormone levels in 30 Finnish men who changed their diet from high to low fat and back to high fat.

In all of the studies, "a diet rich in protein and fat and low in carbohydrate, grain, total and grain fiber was found to be associated with high plasma levels of androgens and estrogens, and higher bioavailability of testosterone and estradiol," Adlercreutz wrote in his paper, "Dietary Factors, Sex Hormone Metabolism and Cancer."

A Western-type diet results in lowering of sex hormone binding globulin (SHBG) in plasma and leads to higher biologic activity of testosterone and estradiol. "This higher biologic activity during long periods of time could stimulate the proliferation of already existing small cancers until they are clinically evident," Adlercreutz wrote.

In addition, the studies found that the intake of

fiber correlates negatively with plasma and urinary estrogens and positively with fecal estrogens. Very low fat intake is also associated with low plasma sex hormones and high fecal estrogen excretion. "The explanation seems to be that a high fiber and low fat diet leads to an interruption of the enterohepatic circulation of estrogens." In women who consume a Western diet, the estrogens may circulate many times, while those who consume a low fat, high fiber diet tend to excrete more of the estrogens.

"In young Finnish women we found that a high dietary fat/fiber ratio was associated with low SHBG and thus high bioavailability of the sex hormones. A Western diet therefore seems to lead both to high sex hormone levels and to higher bioavailability of the hormones."

Vegetarians in the study had lower biologic activity of the sex hormones compared to omnivores. Breast cancer patients and omnivores consumed very similar diets, except that the patients consumed fewer high fiber grain products. The production of estrogens was identical in the omnivores, vegetarians and breast cancer patients in the Finnish study.

In addition, intestinal bacteria play a crucial role in mediating the dietary effects on the hormonal risk pattern. Adlercreutz advised against excessive use of antibiotics and suggested that if one must take antibiotics, to consume foods high in lactobacteria, such as yogurt.

Adlercreutz also studied bile acids in relation to diet. The theory has been that bile acids are carcinogenic and affect the intestinal mucosal cells, causing cancer in susceptible persons. Adlercreutz studied women who changed their diet only by substituting whole grain rye bread for other breads. The proportion of the bile acids that esterified, or were coupled with other substances, was doubled two weeks after women changed their diets.

"Our theory is that the esterified bile acids are not carcinogenic and those who have higher concentration of esterified bile acids in feces are protected," Adlercreutz said.

#### **Microwaved Meat Makes Headlines**

Richard Adamson, director of NCI's Div. of Cancer Etiology, likes to barbecue.

However, Adamson says he is convinced that mutagens caused by high temperature cooking of meat are carcinogenic.

Rather than cut meat from his diet, Adamson hit upon the idea of microwaving steaks, hamburgers, chicken, and ribs, and pouring off the carcinogenic juices before putting the meat on the grill.

"I'm from the Midwest (Council Bluffs, Iowa),"

Adamson told **The Cancer Letter**. "Up until a few months ago I used to eat meat well done. Now I eat it medium."

Adamson made headlines last week ("Microwaved Meat Is Safer To Eat," in "USA Today," was one) after his presentation at the ACS Science Writers meeting in Phoenix.

Over the past several years, Adamson and other researchers in Japan, the U.S., and Europe have conducted laboratory studies of cooked foods. They discovered several new mutagens, called heterocyclic aromatic amines, some of which have been shown to be carcinogenic in animals. Seventeen HAA mutagens have been isolated and most identified through the Ames/Salmonella test and other techniques.

The mutagens are formed from the reaction of amino acids and creatinine, which occurs in the muscle of animals, studies by the Japanese and Lawrence Livermore National Laboratory have shown.

The mutagens were found in high levels in beef, pork, lamb, chicken and fish cooked at normal temperatures used in the U.S. Eggs and egg products, milk, cheese, tofu and organ meats showed little formation of mutagens, except when cooked for a long time at high temperatures.

Negligible amounts of mutagens are formed during microwaving, stewing, boiling or poaching, Adamson said. However, higher temperature cooking methods (above 100 degrees Celsius), such as frying, broiling, and barbecuing, tend to produce the highest amounts of mutagens. Oven roasting and baking produce low to intermediate levels of mutagens. The cooking temperature is more important than cooking time in the mutagen production, Adamson said.

A study in rats found that four mutagens isolated from fried ground beef caused various types of tumors. The most common compound in cooked beef, called PhIP, induced lymphomas in mice and tumors of the mammary gland and large intestine in rats. Three of the compounds, IQ, 8-MeIQx and PhIP, were studied for their absorption and ability to form DNA adducts in monkeys. The studies have shown so far that the compounds are absorbed, IQ and PhIP form DNA adducts, and IQ was found to induce liver cancer in monkeys, Adamson said.

Risk assessments have found that approximately 2,000 additional cancer cases per million over a 70 year period may be due to HAAs.

"These compounds are much more potent than many compounds regulated by the Environmental Protection Agency," Adamson said. "If HAAs were regulated by EPA they would have been banned yesterday."

Adamson provided the following culinary guidelines to lessen the risk of consuming HAAs: vary the method of cooking, eat beef medium instead of well done, microwave more often, especially fish and poultry, microwave prior to barbecuing and pour off the juice in the microwave dish, stew, poach, and boil meat more often, and avoid meat drippings.

## **Kimes Calls Headline On DRG Reaction "Exaggerated Negativity"**

Brian Kimes, associate director for the Centers, Training, and Resources Program in the Div. of Cancer Biology, Diagnosis, & Centers, objected to the headline on a recent article in *The Cancer Letter* which reported on NCI's effort to convince NIH to establish a new study section for clinical research, or add persons with clinical research expertise to an existing study section.

"I want to protest the exaggerated negativity of your headline in the March 8, 1991, issue of *The Cancer Letter* which states, 'NCI Bid for New Clinical Review Panel Rejected; But Invites Researchers to 'Submit Best Ideas,'" Kimes wrote in a letter to the editor.

"The fact is that your headline can do incredible damage to a process that is progressing extremely well in the establishment of a study section focused on clinical oncology research. There has been no rejection by the Div. of Research Grants (DRG); in fact, they have agreed to move in that direction as the number of applications justifies the need for a separate initial review group. NCI is very pleased with the current progress and continues to work very closely with DRG on this problem.

"At a time when we should all be encouraged by the prospects, your headline is tremendously discouraging to the clinical oncology research community and could damage the possibilities for the future. I have received comments to this effect from several cancer center directors. Dr. [Samuel] Broder [NCI director] is committed to supporting innovative clinical research and NCI will do whatever is needed to provide clinical oncology researchers greater access to investigator initiated grants."

*Ed. note: It is difficult to believe that such dire consequences can result from a hasty reading of the headline by someone who does not then read the entire article. This was a report on a discussion by Michael Friedman, director of NCI's Cancer Therapy Evaluation Program. Friedman said, and we reported, that DRG would consider changes to improve review of clinical research applications, provided there were a sufficient*

*number of applications to review.*

*The fact is that DRG did not, at this time, go along with NCI's request for a new study section or a revamped ET2 (Experimental Therapeutics), a request supported by most of NCI's advisors, the division directors, and Broder. Strictly speaking, the request was rejected, but perhaps the headline would have been more appropriate, and accurate, had it said the request was "rejected, for now."*

*The article was not entirely free of negativity. Members of the Div. of Cancer Treatment Board of Scientific Counselors expressed skepticism about DRG's approach; Friedman said that skepticism was "well founded." DCT Director Bruce Chabner pointed out that ET2 gave fundable scores to only 17 percent of clinical grants it reviewed last year. These were only a few of the negative comments made at that meeting.*

## **Healy Confirmed As NIH Director; Priorities To Include Women's Health**

The Senate recently confirmed the nomination of Bernadine Healy as the new director of NIH, nearly two years after James Wyngaarden resigned the post.

President Bush nominated Healy, a 46 year old physician who has been research director of the Cleveland Clinic Foundation, for the position on Jan. 9. Before joining Cleveland Clinic in 1985, Healy served as deputy director of the White House Office of Science & Technology Policy for a year. She also was a staff fellow at the National Heart, Lung & Blood Institute in the early 1970s and has served as a consultant for several NIH committees and advisory panels.

At her confirmation hearing before the Senate Labor & Human Resources Committee, Healy said NIH must nourish a multidisciplinary human talent base. NIH needs a long term plan that outlines research goals based on the public interest, she said, emphasizing her support for the cost management plan that NIH officials are developing in response to Congressional mandate.

Healy also noted the importance of ensuring the integrity of the peer review system, "dealing with problems of scientific misconduct," and managing the conflicts that arise between science and social policy.

Healy said one priority is women's health, and promised to provide \$2 to \$3 million of the NIH director's \$20 million discretionary fund to the newly created Office of Women's Health Research. She said she intends to use the remainder of the discretionary fund to support grants to individual investigators, but did not elaborate.

Healy said she supports a funding rate of 35

percent for approved grants. The rate is currently 24 percent NIH-wide.

Committee chairman Sen. Edward Kennedy (D-MA) said Healy "had a distinguished record of service to the scientific community and to the government as a teacher, researcher, physician, and administrator. She is dedicated to improving the nation's health care system."

Healy is expected to assume the post prior to the April 9-10 NIH budget hearings before the House Labor, HHS, Education Appropriations Subcommittee.

## Wendy Will Case Cancer Fund Invites Grant Applications In Innovative Areas

The Wendy Will Case Cancer Fund Inc. supports one year grants of up to \$30,000 to support promising researchers and help them establish track records.

To date the fund, established in 1983, has awarded more than \$500,000, primarily to new researchers with innovative approaches. More than half have later received grants from NCI, the American Cancer Society, or others on the basis of the research funded by WWCCF.

The Fund invites research applications, with the following stipulations:

--The fund will consider applications for one year grants only, with a budget of \$30,000 or less.

--The fund will not support the salary of the primary researcher, but will support assistants.

--The fund does not purchase equipment, only supplies.

--The fund will not cover overhead costs.

--The same proposal may be submitted to the Case Fund as to the major funders (ACS, NIH, NCI), after failing to receive a grant from them, with a reworked budget to reflect the Case Fund's limitations. Include the NCI or other agency evaluation with the proposal. Generally, the Fund does not consider applications which have not been previously submitted to and reviewed by one or more of these agencies.

--Also submit a paragraph in lay language describing your proposed research and its significance.

--Closing dates for grant submissions are April 1 and Oct. 1. Funding periods begin July 1 and Jan. 1 of each year. Five copies of the proposal are required.

Members of the Case Fund's National Advisory Board are Joseph Bertino, Memorial Sloan-Kettering Cancer Center; Paul Carbone, Univ. of Wisconsin Clinical Cancer Center; Murray Franklin, Union Health Center, Chicago; and Sydney Salmon, Univ. of Arizona Cancer Center.

For additional information contact Robin Shartiag

or Suzanne Schlect at the Wendy Will Case Cancer Fund, Suite 2500, 135 S. LaSalle St., Chicago, IL, 60603, phone 314-704-8638.

## Trial Of Bone Marrow Transplantation For Breast Cancer To Begin In Philly

Four institutions in Philadelphia are cooperating in the first large randomized trial of autologous bone marrow transplantation for metastatic breast cancer.

Hahnemann Univ. Cancer Program, Temple Univ. Cancer Center, Fox Chase Cancer Center, and the Univ. of Pennsylvania Cancer Center have formed the Philadelphia Bone Marrow Transplant Group to conduct a trial to test whether bone marrow transplants in association with high dose chemotherapy can prolong survival and perhaps cure some women with metastatic breast cancer.

U.S. Healthcare, a major national health care insurer, is underwriting the cost of administering the study and has also agreed to pay the cost for U.S. Healthcare members who choose to enter the trial.

It is the first time that a health maintenance organization has "officially provided coverage on an exception basis in order to support experimental therapy in a randomized clinical trial," according to Hyman Kahn, senior medical director of U.S. Healthcare.

Kahn estimated the administrative cost of the trial will be about \$500,000, but said the figure "isn't firm."

The protocol was approved by NCI, but the trial is separate from other protocols being considered by NCI's cooperative group system, for which Blue Cross/Blue Shield agreed to pay some costs.

The number of centers involved in the Philadelphia trial probably will increase, Kahn told **The Cancer Letter**. The Ireland Cancer Center at Case Western Reserve Univ. is interested in joining, he said, as well as others he did not name. "We are encouraging more centers to join," he said.

Kahn agreed to U.S. Healthcare's involvement because, "I recognized that, because of the prevalence of breast cancer and the fact that bone marrow transplantation is increasingly popular around the country, there would be a lot of demand for this, and whether it should be is not agreed upon. Most insurers don't cover it up front, and a lot have been under coercion, if you will, to cover it. It is a toxic treatment, it has a certain mortality of its own. One should have good statistics. But if we don't do something like this, it is going to be anecdotal for another 10 years."

John Glick, director of the Univ. of Pennsylvania Cancer Center, is chairman of the Philadelphia Bone Marrow Transplant Group.

Patients for the study will be drawn from women aged 60 and younger who have not had chemotherapy for metastatic breast cancer. About 400 candidates will be registered by their referring physicians. The referring physicians will treat them with standard, outpatient combination chemotherapy, intended to induce a complete or partial remission.

Patients who demonstrate a complete or partial response will then be randomly assigned to either bone marrow transplantation with high dose chemotherapy or to standard maintenance chemotherapy. A total of 290 patients, 145 in each arm, will be needed.

Patients assigned to receive transplants will be admitted to Hahnemann, Temple, or Univ. of Pennsylvania hospitals and will undergo the procedure, followed by high dose chemotherapy as a continuous infusion over four days, after which the patient's bone marrow is reinfused.

The growth factor GM-CSF will be used to accelerate bone marrow engraftment, reducing the risk of fatal infection.

The trial will also study cost effectiveness and quality of life issues, including physical functioning of patients, psychological well being, social factors, and emotional shock.

## Fax Directory Of Oncologists Offered

"Cancer Fax Directory," a first-ever compilation of fax numbers, addresses, and phone numbers of hematologists, oncologists, and cancer research scientists around the world, is available for \$25 plus \$5 U.S. shipping and handling, from AlphaMed Press, a division of Hippel Cancer Research Center, 4100 South Kettering Blvd., Dayton, OH 45439, phone 513/293-8508 or fax 513/293-7652.

Other cancer related books published recently:

"PDQ User Guide," for help in searching PDQ on the MEDLARS system. Includes software. \$34.95 from National Technical Information Service, 703/487-4650; use order no. PB90-214909.

"What Every Woman and Her Doctor Could Discuss About Ovarian Cancer," and "The Breast Cancer Epidemic in the United States," by Ezra Greenspan, available free from The Chemotherapy Foundation, 183 Madison Ave., New York, NY 10016, phone 212/213-9292. Call for quantity price information.

"Bone Marrow Transplant Directory," by ONS Bone Marrow Transplant Special Interest Group, \$7 from the Oncology Nursing Society, Publications Dept., 1016

Greentree Rd., Pittsburgh, PA 15220, phone 412/921-7373.

"Standards of Advanced Practice in Oncology Nursing," \$7, Oncology Nursing Society (see address under previous listing).

"NIH Consensus Development Conference on Treatment of Early Stage Breast Cancer," report on last year's consensus conference. Free, single copies, available from William Hall, Office of Medical Applications of Research, NIH Bldg. 1 Rm 259, Bethesda, MD 20892.

## RFA Available

RFA OD-91-02

Title: Construction of mouse facilities

Letter of Intent Receipt Date: April 15

Application Receipt Date: May 24

Congress provided \$14.8 million to the NIH Office of the Director for extramural facilities construction grants. The report language cited mouse production facilities in particular. Of this amount, \$4.8 million has been identified for funding two applications that were submitted in response to a previous solicitation and received high priority scores, but were not funded in FY 1990.

Thus, in response to this latest Congressional action, NIH is issuing this RFA to solicit construction grant applications for the construction of large scale mouse production and mutant characterization facilities.

Support may be requested for the construction of new facilities and additions or renovations to existing facilities that will be dedicated to the breeding and production of specialized strains of mice, including inbred and mutant mice, necessary to meet the nation's needs in conducting biomedical research on a broad range of topics. Associated fixed equipment necessary for operation of these facilities may also be requested as part of the application.

Any domestic, non federal public or nonprofit institution, organization, or association that conducts or supports biomedical research is eligible to apply.

This one time solicitation based on the FY 1991 appropriation will make available up to \$10 million for this initiative. Final amount to be determined will be based on the peer review evaluation and the judgement of the NIH Director. Up to 75 percent of the allowable costs of a project may be provided, not to exceed \$10 million.

The matching contributions by the institution may be in cash and in kind, fairly evaluated, including plant and equipment or services throughout the required 20 year period of usage of the facility (and including such specialized strains of mice as the HHS Secretary may request for purposes of biomedical research). Amounts provided by any agency of the federal government, other than HHS, and services assisted or subsidized by any such agency, may be included in the amount of such matching funds.

Prior to grant award, the applicant must provide an assurance of required matching funds and that other funds have been secured to meet any projected costs in excess of the award amount. Requests of less than \$500,000 will not be accepted. No indirect costs will be covered.

A copy of the complete RFA is available from Kenneth Brow, Chief, Research Facilities Branch, Div. of Cancer Biology, Diagnosis & Centers, National Cancer Institute, Executive Plaza North Rm 300, Bethesda, MD 20892, phone 301/496-8534.