THE CANCER NEWSLETTER

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FOUR MORE GRANTS PLANNED BY PROSTATIC CANCER PROJECT THIS YEAR; APPLICATIONS STILL ACCEPTED

The National Prostatic Cancer Project is still accepting applications for grants to be awarded during the current fiscal year. Four awards will be made, in epidemiology, experimental biology, detection and diagnosis, and treatment, bringing to 34 the number of projects funded by NCI's organ site program and operated out of a "headquarters" grant to Roswell Park.

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In Brief

DATA AVAILABILITY FROM CANCER SURVEY PRESENTS PROBLEMS -- WHO GETS IT FIRST, CONFIDENTIALITY

WHO SHOULD have first crack at data compiled by NCI in the third National Cancer Survey (*The Cancer Newsletter*, Aug. 23) – NCI staff members, or non-government researchers? Sidney Cutler, associate director of NCI's Biometry Branch, presented that question to members of the survey advisory committee. The Freedom of Information Act requires NCI to make the information available to anyone who asks. Cutler said some NCI staff members are preparing papers based on survey data and want its release held up until their work is published. The committee left the question open, but the law is clear and NCI may not refuse requests. Computer tapes will be available, at a fee to cover the cost of the tape. . . . **CUTLER'S BRANCH** has been "very unhappy" over publication by the Epidemiology Branch of the county-by-county survey of cancer deaths (*The Cancer Newsletter*, April. 26). It was based on 1960 census data, while Cutler's survey used the 1970 census . . . . **JOSEPH SCOTTO** of Cutler's staff pointed out that the survey turned up only eight cases of angiosarcoma from the 21 million persons covered in the three-year survey. NCI feels the attention to this disease caused by the flap over polyvinylchloride is unwarranted by the incidence rate although agreeing there may be a threat in some occupational specialties . . . . **INVESTIGATORS** will be encouraged to develop any reasonable hypothesis on the association of a variety of factors with various cancers, then test them with a computer run with the survey data. Follow up studies then could be designed to pursue promising leads. Data will be stratified to permit comparisons involving comparable people . . . . **CONFIDENTIALITY** of medical records involved in the survey is posing a problem. Most states prohibit their release by law. Screening names out of the computer produced lists is no problem, but survey advisory committee members pointed out that some investigators will at least have to look at the names in the files. "How else can you determine which names are of Spanish origin if you're doing a study of a Mexican-American population?" one committee member asked. The answer: look at the data in the file room with an NCI staff member present.

PHASE II STUDIES SHOW CYTOXAN, 5FU "LEGITIMATE AGENTS"

(Continued from page 1)

Gerald Murphy, Roswell Park director, is also director of the prostatic cancer project. Under the headquarters grant system, applications are received and reviewed by the headquarters institution – not by NCI. The project director's recommendations must be approved by NCI and the National Cancer Advisory Board, but the NIH study section system is bypassed.

The prostatic cancer project will have $4.2 million to spend in the 1975 fiscal year, based on the appropriations bill approved by the House of Representatives. This could be increased by the Senate's decision to add $60 million over the House figure to NCI's appropriations. No breakdown on where the extra Senate money would go in NCI has been made available yet.

Murphy, in a letter to David Joftes, acting chief of NCI's organ site programs branch, discussed five projects he said "should be highlighted because of their importance and/or progress made."

– Phase II studies of chemotherapeutic agents in prostatic cancer. This study is under way at five participating institutions: M. D. Anderson, with Douglas Johnson principal investigator; Univ. of Iowa, Joseph Schmidt; Hopkins, William Scott; Mass. General, George Prout; and Virginia Mason Clinic, Robert Gibbons.

"This is a singularly important contribution," Murphy said. "A scan of the literature will show that very little had been done in the area of prostatic cancer chemotherapy prior to the initiation of the above study. It is very important to stress the thoroughness of patient evaluation, follow-up and the record-keeping on each patient. Despite the preliminary nature of the accumulated data, both Cytoxan and 5FU have demonstrated advantages and efficacy over standard therapy (palliation) and may be regarded as legitimate therapeutic agents.

– Animal model systems for testing therapeutic agents. This work is being carried out by Donald Coffey, Hopkins, and Avery Sandberg, Roswell Park.

"Although both these investigators would unhesitatingly tell you the deficiencies in their systems," Murphy said, "they might add 'What else do we have?' There are no other systems for testing therapeutic effectiveness. Their systems (combined) have pointed to the therapeutic effectiveness of drugs that are being currently evaluated (5FU, Cytoxan, Estracyt, Streptozotocin)."

– Development of specific cytotoxic agents, by Arnold Seligman, Sinai (Baltimore), and Cecil Robinson, Hopkins. Seligman is developing agents that will become cytotoxic in vivo by action of specific prostatic acid phosphatase. Robinson is developing compounds that will tie up the enzyme 5 alpha-reductase and thereby prevent the conversion of testosterone to the more potent androgen, dihydrotestosterone.

"Although both projects are newly awarded," Murphy said, "you have seen the amount of progress by Dr. Seligman. It is important to ask, 'Who else is developing cytotoxic agents specific for this disease entity?' This is not being done by the pharmaceutical industry, and we have nothing in this order from NCI."

– Evaluation of extended radiotherapy for prostatic neoplasm. This work is being done by Malcolm Bagshaw, Stanford, who is evaluating the hypothesis that metastic spread from the primary site is via the lymphatics and is thus sterilizing the primary site as well as the next higher lymph node group.

"The information or knowledge that will be gained from this study will lead to viable alternatives for early treatment, e.g. surgery vs. radiotherapy, and is relevant to the question posed by a member of the Cancer Advisory Board at our recent review," Murphy said.

– Carcino-fetal antigens in prostatic cancer, by Ming Chu, Roswell Park. "This study has already revealed that human prostatic fluid from prostatic cancer patients, but not from normal controls, contains CEA active fractions," Murphy said. "These results indicate the presence of a tumor specific antigen which may be a CEA or CEA-like substance. Ultimately this work will lead to a practical radioimmunoassay which will be useful for the detection and diagnosis of prostatic cancer."

RAUSCHER TABS OAK RIDGE IMMUNOLOGIST TO HEAD BASIC RESEARCH AT FREDERICK

The basic research program at NCI's Frederick Cancer Research Center will be run not by the "world-reknowned scientist" called for by the National Cancer Advisory Board but by "a young scientist of demonstrated ability and potential."

Michael G. Hanna Jr., PhD, who is director of the Immunology of Carcinogenesis Group at the Atomic Energy Commission's Oak Ridge National Laboratory, has been selected for the prestigious job at Frederick.

Hanna will be on Litton-Bionetics' payroll but was picked by NCI Director Frank Rauscher with the advice of a selection committee that included NCAB members Harold Amos and Harold Rusch. He was one of 18 finalists, screened from an original application list of more than 90, who were asked to submit detailed plans for programs they would initiate if selected for the job.

Rauscher, the selection committee and the NCI Executive Committee all were impressed by Hanna's proposal for programs in immunology and immunogenetics. "Tumor immunology is the hottest thing going right now," Rauscher said.

Hanna's proposal also included a plan to study the

biology of metastasis, a research program in cell differentiation and growth, a program in the immunobiology of viral carcinogenesis, and a program in the immunobiology of chemical carcinogenesis.

An NCAB committee headed by Sidney Weinhouse of Fels Research Institute last year studied the question of how NCI could best use the Frederick facilities and came up with the suggestion that a basic research program should be established, headed by a scientist "of outstanding caliber and stature who could attract other scientists from around the world."

The board accepted the Weinhouse suggestion and asked Rauscher to start looking for such a person.

Rauscher acknowledged that Hanna's appointment was not what the Weinhouse committee had in mind and said he expected to get some criticism. But Rauscher said Hanna is "a young scientist of demonstrated ability and potential, a bright young man who can attract the kind of people we need to develop a first rate program at Frederick."

In fact, Hanna already has signed up three investigators for his team – James Ihle of Oak Ridge who will direct the projects on immunobiology of viral carcinogenesis; Margaret Kripke, Univ. of Utah, who will head the project on immunobiology of chemical carcinogenesis; and Isaiah Fidler, Univ. of Pennsylvania, who will head the program on the biology of metastasis.

Hanna is 38, received his PhD in biology and radiation biology from the Univ. of Tennessee in 1964 and has been at Oak Ridge since then. He has been editor of *Contemporary Topics in Immunobiology* since 1971 and has authored or co-authored five books and 70 scientific papers.

Hanna will work on a part-time basis as a consultant to Litton-Bionetics, which runs the Frederick center under contract with NCI, until next spring when he will assume full-time duties there. It will require up to two years to get the program into full operation, when its budget will be about $2.5 million a year, with 20 scientists and 80 support personnel.

VAN NEVEL NEW NCI INFORMATION CHIEF; KAREL LEAVES FOR JOHNSON FOUNDATION

Frank Karel, associate director for public affairs at NCI, will leave Oct. 1 to become director of information services for the Robert Wood Johnson Foundation in Princeton, N. J. He will be succeeded by his deputy, Paul Van Nevel.

Karel came to NCI two years ago to head up the institute's expanding information program. Van Nevel is a Univ. of Wisconsin graduate, was director of public relations for the university's medical center for four years and held the same position for the Hopkins Medical Institutions for five years before joining NCI 18 months ago.

CARBONE NAMED NCI CLINICAL DIRECTOR, RAUSCHER SHUFFLES TREATMENT ACTIVITIES

Paul Carbone, who has been associate director for medical oncology in the Div. of Cancer Treatment, has been appointed clinical director for NCI, filling one of the two positions vacated by the retirement of Alfred Ketcham.

The other job held by Ketcham, chief of surgery, was filled by the appointment of Steve Rosenberg, of Harvard.

When he named Carbone to the clinical directorship, Rauscher also implemented one phase of his plan to reorganize NCI's scattered treatment activities. That position had been located in the Div. of Cancer Biology & Diagnosis, headed by Nathaniel Berlin; it will now be located in the Treatment division.

In another significant phase of the reorganization, Rauscher has ordered that cooperative clinical trials group leaders report their findings to the Treatment division. The $18 million program is administered by the Div. of Research Resources & Centers. The order is aimed at improving coordination of the cooperative efforts with other treatment research, and to give the Treatment division responsibility for that coordination.

Carbone has been chairman of the treatment committee of the Breast Cancer Task Force, a program administered by Berlin's division. Carbone's connections with the two divisions plus his work with the cooperative groups has enabled him to achieve a degree of coordination in the breast cancer program unusual at NCI.

Ketcham's retirement is effective Sept. 1. He has accepted a position as professor of surgery and chief of the division of oncology at the Univ. of Miami. Gordon Zubrod, former director of the Treatment division, heads the comprehensive cancer center at Miami.

HEW PROPOSES NEW RULES FOR PREGNANT WOMEN, FETUSES, PRISONERS IN RESEARCH

HEW has announced proposed rules to prevent abuses in research on special categories of human subjects.

The proposed rules would augment more general regulations issued last May 30 (*The Cancer Newsletter*, June 7) providing procedural protection for all human subjects in HEW-supported research.

The new rules provide special protection for pregnant women, fetuses, abortuses, prisoners, and the institutionalized mentally disturbed.

Secretary Caspar Weinberger noted that these special measures were originally described in an NIH staff paper published in the *Federal Register* Nov. 16,

1973. "While there was criticism of certain details in the draft, most of the comments supported the idea that we should provide additional safeguards for those groups who have limited or no ability to provide informed consent on their own," Weinberger said.

Additional safeguards to be required under the proposed rules include the establishment of special review groups to assure the reasonableness and validity of consent and to consider the ethical issues involved.

In calling for comments on the proposed rulemaking, Weinberger said that such comments should be particularly useful to the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research which was authorized by the National Research Act of 1974, signed into law by the President on July 12. The act directs the commission to conduct a comprehensive study of the basic ethical principles underlying biomedical and behavioral research and to develop guidelines for the conduct of such research.

The act also places a temporary moratorium on the conduct or support by HEW of research ". . . on a living human fetus, before or after the induced abortion of such fetus, unless such research is done for the purpose of assuring the survival or such fetus."

"All comments received on this matter will be made available to the commission," Weinberger said. "These comments, plus the proposed rules themselves, should provide a good base for the deliberations on the issue of fetal research, on which the commission must report within four months, as well as on the issues raised by the other provisions of the proposed ruling.

The proposed rulemaking appears in the *Federal Register*, Aug. 22. Interested persons have 90 days to comment. Comments, views, and arguments should be addressed to the Chief, Institutional Relations Branch, Div. of Research Grants, NIH, BEthesda, Md. 20014.

RFPs AVAILABLE

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

RFP NCI-CM-53770

Title: *Primary and detailed in-vivo screening for anticancer activity*

Deadline: *Oct. 15, 1974*

Proposals are solicited for primary and detailed in-vivo testing for anticancer activity. Assay systems (tumors and animals), materials to be tested, and protocols for testing will be supplied by NCI.

NCI is seeking the services or organizations which have facilities and capability to house sufficient numbers of mice, to maintain and transplant tumero lines; to prepare materials for testing; to conduct a minimum of 25,000 tests in the L1210 lymphoid leukemia assay plus appropriate controls per year (or the equivalent in work effort in another assay); and to report all test data for computer processing on forms furnished by NCI.

In addition, organizations must also have the capability to conduct testing in in-vivo tumor assays other than L1210, such as P388 lymphocytic leukemia, B16 melanoma, and Lewis lung carcinoma.

The principal investigator must have experience in the in-vivo testing of drugs in rodents. Proposals are invited for a three-year contract period for the L1210 tests, using six mice per test and treating IP QD1-9; at the following levels: 25,000, 37,000, 50,000, and 62,000 L1210 tests per year.

Contracting Officer: George E. Summers Sr.
301-427-7463

RFP NCI-CM-53828

Title: *Study in pharmacology of new antitumor agents*

Deadline: *Oct. 11, 1974*

NCI will make available to interested contractors a request for proposal to conduct studies on the clinical pharmacology of potential anticancer agents. Primary concern will be on the acquisition of data relating to the absorption, distribution, metabolism, and excretion of these agents in man.

Agents selected for study will be those in active Phase I and Phase II clinical trials as determined by the project officer. Any contract awarded hereunder will require adequate assurance of protection of human subjects.

Contract Specialist: D. J. Bowers
Cancer Treatment
301-427-7460

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