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NCAB TO GET NCI BYPASS BUDGET MAY 13; DEVITA TELLS CENTERS THAT IS WHERE "OUR PHILOSOPHY CAN BE FOUND"

For the director of the National Cancer Institute, the year is divided into two seasons. The first extends from mid-May, when the NCI bypass budget is announced for the fiscal year which starts a year from the following October to late January, when the President's

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In Brief

DEADLINE JUNE 1 FOR CANCER RESEARCH INSTITUTE GRANTS; CHABNER TO PRESENT KARNOFSKY LECTURE

IMMUNOLOGY GRANT applicants to NCI and the National Institute of Allergy & Infectious Diseases with priority scores between the projected payline of 158 and 200 have until June 1 to apply for support from the Cancer Research Institute. The Institute announced it would provide interim support totaling $1 million for selected projects jeopardized by the Administration's proposed cutback in the number of NIH competing grants (**The Cancer Letter**, April 19). The support from the private organization will be available even if the Administration relents and goes along with the intent of Congress to fund 6,500 grants this year; the payline still would be about 170-175, leaving some very good research unfunded. Contact Cancer Research Institute, 133 E. 58th St., New York 10022.... **BRUCE CHABNER**, director of NCI's Div. of Cancer Treatment, will present the 16th annual David A. Karnofsky Memorial Lecture May 20 at the American Society of Clinical Oncology meeting in Houston. The title: "The Oncologic End Game." The lecture will be preceded by Sydney Salmon's presidential address, and followed by remarks from NCI Director Vincent DeVita.... **RAYMOND HOUDE**, professor of medicine and pharmacology at Cornell Univ. Medical College and attending physician at Memorial Hospital, has received the 1985 Oscar B. Hunter Memorial Award from the American Society for Clinical Pharmacology & Therapeutics.... **WILLIAM CRIST**, professor of pediatrics at the Univ. of Alabama, will become chairman of hematology-oncology at St. Jude Children's Research Hospital Aug. 1. Crist will fill the vacancy created when Joseph Simone moved up to director of St. Jude.... **STEVEN ROSENBERG**, chief of the Surgical Oncology Branch in NCI's Clinical Oncology Program, will report to the National Cancer Advisory Board May 13 on his research with lymphokine activated killer cells and recombinant interleukin-2 in the treatment of cancer. President's Cancer Panel Chairman Armand Hammer was so impressed with Rosenberg's work that he contributed $100,000 to his program so he could double the number of patients he was treating (from two to four). Since then, NCI has added additional resources to the effort, enabling Rosenberg to treat eight patients.

DEVITA: BYPASS BUDGET IS WHERE NCI PHILOSOPHY ON FUNDING CAN BE FOUND

(Continued from page 1)

budget for that same fiscal year is sent to Congress.

During that first season, Vincent DeVita speaks with all the eloquence at his command, and that is a lot, on the prospects embodied in the bypass budget. His enthusiasm is infectious as he relates each bit of very important progress that can be made, given the amount of money sought for each of those areas. He defends the bypass figures with vigor and is totally convincing in establishing the validity of the amount requested.

The second season starts when it becomes publicly known, once again, that neither DeVita's eloquence and enthusiasm, nor reasonable judgment and good sense, nor the grim toll of cancer nor the prospects for reducing that toll, have had any impact on anyone in the Office of Management & Budget, or on the President.

It is during that second season that DeVita must stop selling the bypass figure and start hustling the President's. The director is a Presidential appointee and can be removed without cause or explanation at any time. But even back in his Public Health Service, tenured position, DeVita was a team player and would never go public against his superiors. The rule of every Administration is that once the President's budget goes to Congress, every agency head must support it--with a smile, if possible.

That has been especially difficult during the second season this year. Not only did the President come in with a request for NCI that was $400 million under the bypass budget for the 1986 fiscal year, but he is trying to take another $48 million out of NCI's pocket in FY 1985 through the multiple year funding maneuver. Bitter stuff to take with a smile.

Occasionally, the agency head who is trying his best to avoid the charge of budget busting will let his guard down and allow candor to prevail. At the recent meeting of NCI staff with cancer center executives, DeVita was asked what NCI's philosophy has been in apportioning funds.

"Our philosophy can be found in the bypass budget," DeVita answered. "We would like to stabilize RO1 and PO1 grants by funding 40 per cent of those approved. We would like to increase the number of centers by 50 per cent by 1990." He pointed out that the Year 2000 plan, built into the bypass budget last year, called for an NCI budget of $2 billion by 1990--twice the current budget.

However, the team player in DeVita surfaced. "There are a couple of things that could be said," he added. "I've been managing the NCI budget for five years, and I can tell you it is a lot easier to manage without inflation. If we can reduce the national deficit and if the economy continues to grow, we'll get what we need. I think Congress will reduce the deficit, and that the economy will continue to grow. That's why I say don't restrict your planning on the basis of the present budget."

Referring to the cancer center core grant guideline revisions which had been presented to the center representatives earlier, DeVita said, "The process of revising center guidelines affects a lot of people all over the country. It's not something you can wake up in the morning and say we'll do it."

The multiple year funding scheme affects centers as well as RO1 and PO1 grants, DeVita noted. OMB directed that one core grant of those being renewed this year be funded for two more years, which takes $1.2 million from the 1985 budget. He did not mention, but it has become known, that OMB has ordered that no new core grant be awarded this year. That will affect the Univ. of Maryland Cancer Center, whose application had a priority score in the fundable range.

DeVita discussed his emphasis on centers taking the lead in regional cancer control activities. "If you think survival data are not important, you're not paying attention to what goes on in Congress. When survival for patients at many centers for some cancers is higher that we're seeing from our SEER data (national figures); when there is cancer that could be prevented and isn't; when there is treatment that could be given and isn't; when there are underserved areas not being served; when we're not doing treatment around the country as well as we should; when administration of the halfway technology we have is not being done effectively; cancer centers can help. I don't mean to put the entire burden on centers, nor that we will abandon research. But centers can take the lead. I believe we should increase the centers program. There are jobs out there we're not doing very well. Research, we are doing well."

Charles Moertel, director of the Mayo Comprehensive Cancer Center, responded, "The point is, how do we bring the best care into areas where it doesn't exist? Centers do have the wherewithal to promote it, but it is very difficult to do under the present guidelines. The cancer control research requirement is too restrictive. Control as such, without research, has been wiped from centers' responsibility. If you would get centers back into cancer control as such, centers could do the job."

DeVita said the Community Clinical Oncology Program, with centers participating as research bases for some, "is an ongoing experiment" in cancer control. "It's still too early to know if it works, in the treatment area."

The 1987 fiscal year bypass budget will be

presented to the National Cancer Advisory Board May 13. DeVita and his staff have had an especially difficult time this year in developing the budget, considering the shambles the Administration has made out of planning efforts. Congress is not likely to accept the cuts in the NIH and NCI budgets proposed for the 1986 fiscal year by OMB, yet the Institutes have to assume that the OMB figure is all they are going to get until the congressional appropriation is enacted. Trying to predict what will be needed in 1987 when there is such a big gap between what Congress probably will approve and what the Administration asked is not easy.

The bypass budget has been a target of critics of the National Cancer Act of 1971 in the past, and the White House and Dept. of Health & Human Services would dearly love to eliminate it this year. They are not comfortable with permitting an agency to tell the world, including Congress, what it really needs to do the best job possible, and then submitting a much lesser request. It puts them in a no-win situation—cutting cancer research is not something a President or HHS secretary wants against him/her in the history books. Yet competing demands on the health budget, being expressed by forces which outnumber cancer constituents, forces the Administration into that position.

That is exactly why those wise individuals who did the spadework that led to the National Cancer Act of 1971 wanted to give NCI some independence in the budget process. It was their intent that the bypass budget would be the only budget for NCI that Congress would get.

So the grim second season is about to end, and DeVita and his staff once again will have the opportunity to talk with enthusiasm about the needs and opportunities of the National Cancer Program, including spelling out the money required to adequately pursue those opportunities.

They did that brilliantly last year, by tying the bypass budget to the Year 2000 Plan, an effort that included two price tags—the cost in dollars to reduce cancer mortality by half by 2000 AD, and the cost to the country, 225,000 lives a year, if that money is not forthcoming.

More than 45 days have passed since the Administration submitted its rescision request to Congress that would trim $4.3 million from NCI's 1985 budget. Since no action was taken by either house, that rescision is dead. The money was taken, as Congress had ordered, from travel and hiring of consultants. The rescision may be resubmitted, however, since it had been done as Congress had ordered. Failure to act on it was due more to Congress being tied up with other matters than with hostility to the rescision.

RETROVIRUS VACCINATION FEASIBLE, WORKSHOP PARTICIPANTS CONCLUDE

"The consensus of the workshop participants... was that prevention of retrovirus diseases through vaccination is feasible and that basic studies are required in various areas," a report on the workshop held by the Biological Carcinogenesis Branch of NCI's Div. of Cancer Etiology concluded.

The report was presented by Padman Sarma, program director for RNA virus studies, at the last meeting of the DCE Board of Scientific Counselors. The workshop was chaired by Hilary Koprowski, director of Wistar Institute and a member of the DEC Board. Excerpts from the report follow:

Some general principles apply to most virus vaccines for use in the prevention of human disease. Neither vaccination nor recovery from natural infection always results in total protection against a later infection with the same virus. This situation holds true for diseases for which successful control measures are available, including poliomyelitis, smallpox, influenza, rubella, measles, mumps and adenovirus infections. Control can be achieved by limiting the multiplication of virulent virus upon subsequent exposure and preventing its spread to target organs where the pathologic damage is done (e.g., polio and measles viruses kept from the brain and spinal cord; rubella virus kept from the embryo).

Killed virus vaccines which elicit circulating antibodies against viral coat proteins confer an immunity of short duration, necessitating repeated immunizations, often with undesirable side effects such as hypersensitivity. While IgG and IgM antibodies are induced, IgA antibodies at the portal of virus entry are not induced. Live viruses prepared as attenuated viral vaccines multiply in the host and induce an inapparent infection simulating natural infection. They stimulate longer lasting protection via humoral and cellular immunity, and induce resistance at the portal of virus entry through induction of IgA antibodies. The drawbacks of live attenuated viral vaccines include the possible presence of unrecognized adventitious agents latently infecting culture substrates, and reversion of the attenuated virus to virulence. These problems can be safely controlled by the use of suitable culture substrates (e.g., human diploid cell lines) and by appropriate monitoring techniques. Several live human viral vaccines have been in use for years and have been safely administered to millions. While previous methods of deriving attenuated virus strains depended to a large extent on the passage of virus in various hosts and cell cultures, the current search for attenuated strains is being approached by laboratory manipulations

aimed at specific genetic alterations in the virus. These include host range mutants, temperature sensitive mutants, cold adapted mutants, deletion mutants, and a variety of genetic recombinants.

Synthetic vaccines such as antigenically active polypeptides have been prepared for hepatitis B, influenza, and polio viruses. They have induced neutralizing antibodies in animals. However, the synthetic peptides have been weak antigens, and a search for potent and safe adjuvants is under way. Conformation of these peptide antigenic determinants appear to be even more important than their amino acid composition and sequence. On this same basis, anti-idiotype antibodies which apparently present antigenic determinants in the native conformation are able to enhance antibody formation upon subsequent injection of a subimmunogenic dose of antigen, and even induce weak antibody response by themselves alone. . .

Retroviruses spread in essentially three fasions: horizontally between animals; vertically as congenital infection; or genetically as viral genes on chromosomes. Laboratory mice of different strains reveal one or more of all three modes of transmission, whereas cancer inducing retroviruses of wild mice, cats, cattle and man are principally transmitted by the horizontal route. Known mechanisms of viral pathogeneis/oncogenesis are: (a) influence of LTR in determining tissue specificity, virus regulation and virulence; (b) viral envelope mediated pathogenicity; (c) transacting transcriptional activation through proteins coded by the LOR region of viral genome; and (d) virus mediated transduction of cellular onc gene sequences. Mammalian retroviruses such as the leukemia/sarcoma viruses of the mouse and cat are similar, cause a similar spectrum of diseases and reveal similar levels of virus expression (varying from overt to covert). The newly identified retroviruses in cattle (bovine leukemia virus-BLV) and man (human T-cell lymphotropic viruses—HTLV) have similar characteristics, are intimately cell associated, and exist in the host tissues in a highly repressed state. A transacting p42 protein encoded by the LOR region of the genome of the virus apparently brings about cell transformation through transcriptional activation mechanisms. HTLVs and BLVs may form a separate group of retroviruses.

HTLVs have a predilection for T4 cells, primarily determined by the presence of a cell surface receptor specific for HTLV. HTLV-3 apparently also infects non-T4 cells and has a brain reservoir (gial cells). Possible control of HTLV may be through blocking and/or elimination of T4 cell receptors (perhaps via monoclonal antibodies) and immunosuppressive components of virus (conceivably P15E). The most immunogenic proteins coded by the env gene of HTLV-1 and HTLV-3 are gp61, and gp120 respectively. Antibodies against these proteins are consistent and are the best markers for sero-diagnosis; however, there is no evidence that they are protective. Deglycosylated forms of these proteins react equally well with human antibodies. HTLV-like viruses occur in macaque monkeys. This nonhuman primate could be valuable for testing vaccines against HTLV and the SAIDS retroviruses.

Lentiviruses (Visna and Maedi viruses of sheep and the equine infectious anemia virus) illustrate the capacity of this group of cytopathic retroviruses to undergo antigenic drifts, similar to the influenza virus, and thus have the ability to escape from the host immunosurveillance system. This feature is especially important in considering vaccination approaches, inasmuch as HTLV-3 appears to have many of the characteristics of lentviruses.

Two presentations emphasized the importance of passive immunity in protecting hosts against retroviral infections. Infant wild mice infected with mouse amphotropic retrovirus postnatally via suckling infected mothers milk can be successfully prevented from getting neurologic disease and lymphoma by repeated passive administration of protective antibodies. Similarly, colostrol antibodies efficiently protect the calf or the lamb, even when challenged with a high infectious dose of BLV material. Both of these observations demonstrate that protection of animals at risk via vaccination can eventually be achieved.

Vaccination of cats with soluble tumor cell antigen vaccine derived from the FL74 feline lymphoma cells proved successful in preventing the induction of feline leukemia virus (FeLV) infection upon challenge with virulent FeLV. RID-PAGE analysis has revealed both env (gp70 and p15E) as well as gag components (p27) in the vaccine preparations. It is not known at this time which of the vaccine component(s) is actually responsible for conferring protection. . .

The immunogenicity of synthetic peptides can be considerably enhanced by coupling with carriers. The methods for preparing various liposome-peptide conjugates was discussed. Covalent linking to the surface of liposomes containing an exposed functional group was found to be the most suitable for immunization using a synthetic peptide fragment of hepatitis B virus envelope protein.

A vaccine should be safe and effective. To improve on currently available vaccines such as killed and live virus vaccines, several elegant approaches are now being evaluated for use as potential vaccines in systems such as influenza, hepatitis B, herpes, and foot and mouth disease. One of these approaches involves the use of expression vectors for selected viral genes. Recent advances in

genetic engineering have made it possible to introduce foreign genes such as nonvaccinia viral genes, coding for proteins involved in inducing protective immunity, into vaccinia virus vectors. Expression of these foreign viral genes has been obtained without impairing vaccinia viral infectivity by using vaccinia promoters. Animals with successful takes of the recombinant vaccinia virus mount humoral and cell mediated immune responses against the proteins of the nonvaccinia virus as well as vaccinia virus and are protected against the challenge with respective nonvaccinia virulent viruses. Some of the problems to be addressed in using the vaccine virus vector expression system are getting a satisfactory vaccine take, and ensuring that the recombinant vaccine has not undergone alterations in tissue tropisms and/or increase in its pathogenicity.

Bacteria, yeasts and certain permanent mammalian cell lines have been genetically engineered to synthesize components of subunit vaccines for several viral infections. In the case of hepatitis B surface antigen (HBsAg) which is the immunogenic and protective protein of this virus, E. coli bacteria, which were transfected with the gene encoding HBsAg, produced small amounts of poorly antigenic material. Yeasts similarly transfected produced intracellular HBsAG particles releasable by cell lysis. This antigen induced a protective response in chimpanzees subsequently challenged with hepatitis B virus. Mammalian cells such as Chinese hamster cells similarly transfected with the HBsAg gene produced large amounts of glycosylated and unglycosylated polypeptides characteristic of plasma derived HBsAg. This antigen also induced a protective response in chimpanzees subsequently challenged with hepatitis B virus.

In similar experiments, the glycoprotein D (gD) of Herpes simplex virus (HSV), the major immunogenic protein, was prepared as a subunit vaccine by expression in permanent lines of mammalian cells through transfection with the cloned gD gene. Secreted proteins were highly immunogenic and afforded protection to mice and guinea pigs against lethal challenge with HSV-1 and HSV-2.

Antigenic variation, a problem associated with influenza viruses, foot and mouth disease viruses and the lentiviruses, has been one of the main causes of vaccine failure. To combat this problem, vaccination with an antigen common to the variants should be considered. Preliminary work along these lines was reported for the FeLV. Using a monoclonal antibody capable of neutralizing most FeLV isolates, a 43 base pair DNA fragment encoding 14 amino acids of FeLV gp70 was identified as a possible cross reactive neutralizing antigenic site of the FeLV gp70 env gene. This 14 amino acid peptide prepared through chemical synthesis was conjugated to a protein carrier and appeared to be promising as an immunogen in priming cats for subsequent booster immunization with killed FeLV. In a search for protective epitopes of the hepatitis B surface antigen, chemically synthesized peptides, predicted from the nucleotide sequence of the S and pre-S genes of HBV were found to be useful to map the native hepatitis B surface antigen (HBsAg) particle, for major subtype and group specific determinants. The immunogenicity of the synthetic peptides is being evaluated in the chimpanzee model of HBV infection as well as in the woodchuck hepatitis virus model.

The viral envelope of FeLV apparently determines the degree of virulence of FeLV in cats. Upon removal of enhancer elements in the LTR, subgroup A FeLV continued to be virulent, whereas such manipulation of subgroup B and C FeLV converted them into nonpathogenic strains. A subunit vaccine consisting of envelope glycoprotein of subgroup A FeLV prepared in yeasts, conferred some degree of protection in kittens against challenge with subgroup A FeLV.

Carbohydrate side chains of viral envelope glycoproteins appear to protect virions from attack by the immune system presumably by acting as decoys. Thus, deglycosylated retrovirus virions induced a better neutralizing antibody response in rabbits than did untreated virus; in addition, such deglycosylated virions absorbed neutralizing antibodies efficiently.

A satisfactory vaccine for feline leukemic virus consisting of inactivated virus and cell membranes is currently available and will be marketed commercially. An experimental vaccine is also currently being evaluated. This latter vaccine which appears to confer protective immunity in cats, was based on the use of micellar like structures called ISCOMS, prepared from the bark of a South American tree. ISCOMS form cage like membranous structures into which membrane proteins of virus can be inserted, thus forming an artificial virus like structure. Proteins are thus presented in a natural array to the immune system and need no adjuvant for eliciting antibody response.

The potential advantages of vaccination with anti-idiotype antibodies: they are not foreign antigens, have no viral or other infectious agents present, combine with antigen specific lymphocytes, stimulate their expansion and stimulate antibodies of broad specificity. Anti-idiotype antibodies may be particularly advantageous for infants and small children who do not respond well to immunization with certain antigens (e.g., certain bacterial antigens) and in those cases where there is insufficient antigenic mass (e.g., filarasis, trypanosomiasis). The efficacy of anti-idiotype

antibodies against rabies was attested to by the finding that mice primed with it and subsequently faccinated with a nonimmunizing dose of rabies vaccine were protected against lethal challenge with the rabies virus. From the standpoint of safety to human subjects, anti-idiotype antibodies may have an as a safe immunogen for the HTLV family of viruses.

Prerequisite knowledge needed for the development of effective retroviral vaccine includes natural history studies of retroviruses; pathogenicity studies of the virus, including definition of the portal of entry, and entry virus-target cell interactions; definition of immune effector mechanisms such as humoral, cytotoxic and other immunoregulatory responses; determination of the role of lymphokines in the regulation of virus infection; and the development of quantitative assays to measure antibody response and expression of virus. There is an urgent need to identify protective immunogens for HTLV-1, 2 and 3 and to identify individuals who have successfully controlled their HTLV infections. Humoral antibodies detected in people with HTLV-3 infections are apparently not protective. The problem of antigenic variation should be considered, especially with respect to HTLV-3. A quantitative virus neutralization test is urgently required to evaluate the virus neutralizing antibody responses against HTLV variants. Animal model systems offer an excellent approach for studies of host immune responses to viral infections as well as studies of viral vaccine efficacy. Present and future approaches to development of vaccines for HTLV type viruses should consider the promising approach of using ISCOMBS as well as consider the use of appropriate expression vectors, such as an adenovirus, where the nonessential genes can be replaced with HTLV genes encoding protectivef env proteins.

The consensus of the workshop participants evident through discussions at the workshop and from letters subsequently received was that prevention of retrovirus diseases through vaccination is feasible and that basic studies are requeired in various areas such as developing animal models for studying vaccination approaches and efficacy; virus-host interaction studies, including studies of host immune effector mechanisms; studies to enhance immunogenicity of vaccine preparations; and the use of diverse modern approaches for vaccine preparation.

Members of the DCE Board who participated in the workshop in addition to Koprowski were Charlotte Friend, Marcel Baluda and Myron Essex. Presenters and moderators were Joseph Melnick, William Jarrett, Essex, Satvir Tevethia, Richard Lerner and Dani Bolognesi.

NATIONAL COALITION ON CANCER AN EDUCATION GROUP, ULTMANN SAYS

"We are basically an education group, to present a unified voice to appropriate bodies on the current state and needs of cancer research. We are seeking support of the National Cancer Program to a level appropriate to past results and present promise."

John Ultmann, chairman of the new National Coalition for Cancer Research, thus stated the character and goals of the group which includes most of the relevant professional societies and organizations.

Ultmann, director of the Univ. of Chicago Cancer Center, said that primary targets for the Coaltion are renewal of the National Cancer Act and adequate funding of the National Cancer Program through appropriations for NCI.

"The Coalition has examined the plan for the Year 2000 and feels that only a major thrust in funding can result in realization of goals so well expressed in the plan and so worthy to be achieved," Ultmann said. "When the original cancer plan was conceived and later implemented with substantial budget increases (following enactment of the National Cancer Act of 1971), it could hardly be predicted what terrible toll inflation would have on real dollar growth of NCI and NIH. But more importantly, it could hardle be imagined what the product of the research effort would be in the mid 1980s—the information explosion about normal and abnormal cells; the major discoveries in the etiology of cancer, particularly in viruses; DNA repair process; identification of high risk groups, such as AIDS victims and HTLV-3; early diagnosis; hybridoma technology; and a host of effective therapies.

"It is our purpose to bring all this information before the public and its representatives so that they can make informed decisions regarding financial support for these endeavors now," Ultmann concluded.

ST. JUDE OFFERS THREE FELLOWSHIPS TO PhD, MD CANCER INVESTIGATORS

St Jude Children's Research Hospital offers three fellowships to investigators seeking further experience and expertise in cancer research. The application deadline for all three is Sept. 1, with the selections to be made by Nov. 1 and starting date of July 1, 1986.

The Karnofsky Fellowship in Cancer Research is offered each year to investigators with either a PhD or MD who are beyond the junior level of accomplishment and would like to gain further expertise in cancer research by collaborating with a member of the St. Jude faculty. Research topics currently

under investigation include drug resistance, oncogenes, hematopoietic stem cell differentiation, red cell aging, cancer clinical trials, oncopathology, monoclonal antibodies and experimental bone marrow transplantation.

Awards are made for one or two years with an additional year negotiable. The fellowship was established in memory of the late David Karnofsky, who as chief of medical oncology at Memorial Sloan-Kettering established worldwide recognition of the importance of chemotherapy in treatment of cancer. Karnofsky was a member of the St. Jude Scientific Advisory Board.

The Journey Fellowship in Biomedical Research is open to a junior investigator with an MD or PhD who seeks experience in one of the specialty areas of research available at St. Jude—biochemistry, immunology, human tumor cell biology, pharmacology virology and molecular biology, pharmacodynamics, pediatric oncology, hematologic malignancies, and child health sciences.

Journey fellowship awards are made for one or two years with an additional year negotiable. Awards are based on merit, recommendations and promise of a productive career in biomedical research.

The Journey Fellowship was established to honor the late Leon Journey, distinguished cell biologist and electron microscopist who served on the institution staff for 10 years.

The Levy Fellowship in Cancer Medicine is offered annually to a physician investigator planning a career in cancer medicine. Levy fellows train in one of the specialty areas of research emphasized at St. Jude—hematologic malignancies, pediatric oncology, infectious diseases, nutrition, cancer pathology, human tumor cell biology, biochemistry, immunology, pharmacology, and virology and molecular biology.

Levy Fellowship awards are made for one or two years with an additional year negotiable. The award is made in memory of Memphis businessman J.L. Levy.

Send inquiries to Director Joseph Simone, St. Jude Children's Research Hospital, PO Box 318, Memphis 38101.

NCI STARTS NEW REVIEW OF CLINICAL TRIALS; "WHAT'S RIGHT, WHAT'S WRONG"

The Cancer Therapy Evaluation Program in NCI's Div. of Cancer Treatment has completed the first of its reviews of clinical trials, a process which is expected to go on for 18-24 months and include as many as a dozen diseases.

The initial disease reviewed was testicular cancer, with several of the leading investigators in that area spending a day at NCI discussing with staff the current situation in that area. "We want the best people in each field to tell us what is right and what is wrong with clinical trials," CTEP Director Robert Wittes said. The next review is scheduled for the first week in June, for non-small cell lung cancer.

Wittes discussed plans for the review with the DCT Board of Scientific Counselors at its last meeting. He noted that the last review of clinical trials by NCI was carried out in 1979. "That was motivated by the question of whether clinical trials groups were doing as best as they could. The report was written by a committee of the Board and became known as the Salmon Report (Sydney Salmon chaired the committee. It was later published as a book, "Cancer Research: Impact of the Cooperative Groups," edited by Barth Hoogstraten). Basically, that was a review of clinical trials groups, particularly the cooperative groups. It was a useful compendium of clinical trials. It was not a critical review, and I don't think it was intended to be.

"Some criticism (in the Salmon Report), was directed to the coordination of clinical trials by DCT," Wittes continued. "It was said that coordination was not as good as it could be because different funding mechanisms were involved, and review was not consistent. Because of the report, it was decided to convert all clinical trials groups to cooperative agreements, except for developing phase 1 and 2 studies.

"Now, the motive with this review is to see how well we're doing, looking over the past five years. How good is the quality of clinical trials? Can we take the system as is and make it better? Can we avoid unnecessary duplication, and define what that is? Can we make sure the system is as lean and informative as it can be? We'll cover the spectrum, from the highly curable to the miserably refractory. We will ask if major questions are being addressed in a major way. If not, then what is the problem? What are the relevant research issues and how well are these being addressed?"

Wittes added, "The issue of who is supposed to judge this is interesting. It is important to get groups of people not involved in the process. That is possible, but it's not the same as bringing oncologists from another planet or country."

"The important question we are trying to answer," DCT Director Bruce Chabner said, "is, are we identifying relevant questions, or just varying a theme on drug combinations? Are groups willing to do new things, not mundane trials? Are they adapting?"

The report of the testicular cancer committee will be completed sometime during the summer. Whether it will be published and where has not been determined, Wittes said, but it will be publicly available.

COLUMBIA CANCER CENTER RECEIVES $1 MILLION, FIVE YEAR ACS GRANT

The Columbia Univ. Comprehensive Cancer Center has been awarded a $1 million, five year grant from the American Cancer Society for a coordinated interdisciplinary investigation into the causes and prevention of cancer, Director Bernard Weinstein announced.

Weinstein, who is principal investigator for the grant, said that in the project, a few specific types of human cancer—lung, cervix, skin and bladder—will be examined by a team of researchers with expertise in a broad range of disciplines: epidemiology, clinical science, pathology, chemical carcinogenesis, molecular virology and molecular genetics. The same case material will be studied by a variety of laboratory methods.

"I am very excited about this grant because it allows us to bring together the wealth of talent we have here to mount a coordinated approach in understanding human cancer causation," Weinstein said. "Since there is evidence that the majority of human cancers are due to external factors, the types of information obtained through the support of this grant will provide important clues to effective strategies of cancer prevention."

Weinstein noted that the techniques of molecular cancer epidemiology were developed at Columbia to complement the animal tests and short term tests that are widely used in cancer research. The techniques combine epidemiologic methods with laboratory techniques that measure specific biochemical and molecular factors of human tissues and biologic fluids.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-57722-09
Title: Preclinical pharmacology investigations of antitumor agents
Deadline: Approximately July 20.

NCI's Developmental Therapeutics Program, Div. of Cancer Treatment, is seeking organizations having the necessary experience, scientific and technical personnel and facilities to conduct a range of preclinical pharmacology studies on antitumor agents or substances of interest in animals.

The studies may involve the development of quantitative methodology for the measurement of drug and/or metabolite in animal body fluids and tissues; stability studies of the drugs in biological milieux; blood level studies in animals; bioavailability studies after oral administration; tissue distribution and excretion studies and structural determination of metabolites and drug transformation products.

The government will supply all animals, drugs, radiolabeled drugs, etc. Contractors will be expected to provide all equipment, solvents, reagents and animal facilities needed to conduct this type of work.

It is anticipated that more than one award will be made for three year incrementally funded contracts as a result of this RFP. Offerors will be requested to submit proposals at two levels of effort for each year of the contract, namely 3.5 staff years and 1.75 staff years. Only one award will be made to an institution.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and was reported in The Cancer Letter Nov. 2, page 7.

Contract Specialist: William Roberts
RCB Blair Bldg Rm 228
301-427-8737

Correction: Support services for the Diet, Nutrition & Cancer Program—RFP NCI-CN-55474-10

Availability of this RFP was published in The Cancer Letter April 12. NCI has added the information that it is a 100 per cent small business set aside procurement.

NCI CONTRACT AWARDS

TITLE: Collection & evaluation of human tissues and cells from patients with an epidemiological profile
CONTRACTOR: Univ. of Maryland, four years, $1,924,996.

TITLE: Metropolitan Detroit Cancer Surveillance, Epidemiology & End Results Program (SEER)
CONTRACTOR: Michigan Cancer Foundation, five years, $11,178,048.

The Cancer Letter _Editor Jerry D. Boyd

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