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NCI To Support Research And Development Of Image Guided Therapy For Prostate Cancer

NCI plans to set aside $13.6 million over the next four years to stimulate collaborations between academia and industry to develop non-invasive imaging technologies for diagnosing and treating prostate cancer.

The NCI Board of Scientific Advisors unanimously approved the Institute's plans for the grants program at a meeting last month. The program would fund eight grants in image-guided therapy.

"Leaders in the field of prostate cancer treatment, including prominent urologists and radiation oncologists, tell us that they want new and alternative methods for dealing with this disease," said Daniel Sullivan,

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In Brief:

Healy Named President, CEO Of Red Cross; AMA Supports Annual Mammograms For 40+

BERNADINE HEALY, dean of the Ohio State University College of Medicine and Public Health and former NIH director, was appointed president and chief executive officer of the American Red Cross. Healy, a cardiologist, succeeds **Elizabeth Dole**. Healy, 54, had surgery last February to remove a cancerous brain tumor, according to news reports. She was the first female NIH director, a position she held from 1991 to 1993. . . . **AMERICAN MEDICAL ASSOCIATION** last week recommended that women get yearly mammograms starting at age 40 to screen for breast cancer. The AMA previously advocated screening every one to two years for women in their 40s. The AMA's Council on Scientific Affairs said the cost-effectiveness of screening younger women is in line with that of other diagnostic procedures. . . . **MARK GREENE**, a medical oncologist at the Mayo Clinic in Scottsdale, AZ, will return to NCI as chief of the new Clinical Genetics Branch in the Division of Cancer Epidemiology and Genetics. Greene was at NCI from 1975 through 1985 first as a staff associate, then a senior investigator, and finally, deputy branch chief, in the former Division of Cancer Etiology. Greene played a central role in developing the research program of the Environmental Epidemiology Branch, which provided the nucleus for the DCEG. Greene has served as a clinical investigator with several clinical trials cooperative groups and as a collaborator in the University of Arizona Cancer Center's Skin Cancer Chemoprevention program project grant. He served as the principal investigator for the Mayo Cancer Center's Familial Cancer

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NCI To Support Network For Image Guided Therapy

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associate director of the NCI Diagnostic Imaging Program. "Methods that are minimally invasive might avoid complications such as impotence and urinary incontinence, which sometimes arise with current surgical or high beam radiation treatments."

Excerpts from the text of the concept statement follow:

Imaging Techniques for Early Prostate Cancer. Concept for a new RFA, eight R21/R33 awards, estimated cost $13.6 million over four years. Program director: Barbara Croft, phone 301-435-9025, email: bc129b@nih.gov

The purpose of this RFA concept is to stimulate research into the development and application of improved imaging methods for the localization, biopsy and minimally invasive delivery of therapy for prostate cancer. Relevant investigations could include technology development, in vitro laboratory work, pre-clinical animal studies, or early feasibility testing in humans depending on the maturity of the methods proposed. It requires the development of several methodologies and their optimization for this particular organ system. The specific goals include the development and application of the following inter-related components: (a) means for measuring local extent of disease using anatomic, metabolic or alternative novel imaging methods, (b) means for improved image guided biopsy and staging or identification of aggressive cancers by metabolic or alternative novel imaging methods, and (c) means for navigation, control of IGT and measurement of early biological effects.

Image Guided Therapy systems. IGT systems typically have several major components: (a) the therapeutic object or target organ, (b) the virtual object which is the generated 3D image of the organ, (c) the navigational device which includes the probe or therapy delivering system, (d) a computer image display system(s) for visual guidance, and (e) a feed back mechanism for control of the therapy process and, when applicable, some means for measurement of early biological effects. For example, in a brain tumor situation, (a) the therapeutic object is the brain tumor, (b) the virtual object is the segmented rendition of the tumor from pre-operative MRI, CT or PET images, (c) the navigational device might be light emitting diodes in the handles of the surgical instruments and TV cameras overhead to detect the laser beams, (d) the computer display system might be a TV monitor in front of the neurosurgeon or a head-mounted display, and (e) the feedback mechanism would be an intraoperative contrast-enhanced MRI image indicating in real-time whether all of the tumor tissue had been removed. A key issue is that the navigational device requires the virtual object to be accurately registered to the therapeutic object. Considerable bioengineering expertise must be combined with basic science and clinical input in designing and developing IGT systems.

Improved localization, image guided biopsy and staging methods for early prostate cancer. Important areas for investigation would include any of the following areas. Improvements in MRI and MRSI methods such as: (a) specialized radio frequency (RF) transmit and receive coils, RF pulse sequencing and 3D imaging methods to improve signal to noise (SIN) and image contrast, and (b) development and application of novel MR contrast materials for identification of prostate cancer. Improvements in TRUS such as novel probe design, RF pulse sequencing, contrast materials, 3D imaging methods, and multi-spectral imaging to improve S/N and image contrast. Advances in PET or SPECT imaging using novel radio-ligands specific for prostate cancer to improve tumor localization and staging. Other novel imaging methods such as optical technologies should be also explored to improve image-guided biopsy and staging of cancer. Image processing methods must be further developed for improved image registration, image fusion, image contrast and resolution. Similarly, improved and, ideally, automatic image segmentation techniques for the prostate gland and surrounding tissues must be developed for determining the boundary of the prostate gland, connective tissues and proposed treatment area. Multi-spectral analysis or computer classification methods as applied to MRI, MRS, TRUS, radio frequency (RF) or other sensor images/spectra are important to explore for classification of tissues as normal, cancer, or the level of cancer aggressiveness. Finally, the possibility of combining these methods with

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PSA or other markers for improved staging of prostate cancer and patient selection for IGT should be explored.

Image Guided Therapy Methods. Energy in a variety of forms can be delivered to a volume of tissue and completely kill all the cells in the treatment volume. Cellular proteins can be coagulated by heating the tissue directly with controlled temperature probes or lasers, or killed by freezing with small probes (cryosurgery). Similarly, chemotherapeutic agents, such as gene therapy vectors, or toxic chemicals can be delivered directly into tumors by small catheter-based tools, or administered systemically and deposited locally by the addition of externally applied energy such as focused ultrasound. Focused ultrasound waves, radiowaves, or microwaves can also be used to heat tissue and cause protein coagulation. Externally focused energy methods are particularly attractive in that no needle or probe has to be inserted into the tissue, and there is potentially more control over the distribution and amount of heat generated throughout the treatment volume. In all of these therapeutic methods, image guidance is required in terms of both navigation of the focal point of the therapy and to control the local degree of therapy. At the recent NCI-sponsored workshop on IGT, it was concluded that all the minimally invasive locally ablative therapies are still under development and should not be prejudged as to their effectiveness relative to each other or to existing standard therapies. These localized therapy methods, coupled with image guidance, hold great promise for minimizing surgical trauma, recovery time, and associated health costs for treatment of prostate cancer and thus their development and feasibility resting should be investigated under this RFA.

Some of the key limitations to widespread clinical use of IGT have been: (a) difficulty in accurately controlling the delivery of therapy to the desired tissue, (b) difficulty sparing normal tissue, monitoring and controlling tissue damage created by the therapy, (c) lack of validation and standards for IGT, and (d) complexity of the user interface. Specific technical problems that need to be addressed include the design, optimization, and validation of all the engineering components of the navigational system and the means for controlling therapy delivery and monitoring of early biological effects. IGT systems need to be developed for the specific application to the prostate, and address the navigational and control scales required for this small gland and associated surrounding critical tissue structures. Similarly, for instances where physical probe insertions are required, the integration of models for incorporating soft tissue characteristics into the IGT system needs to be investigated, since prostate tissues can be deformed.

There is a need to improve methods to control localized therapy. For example, MRI can provide both high spatial resolution and tissue temperature measurement. There is a need to further develop and model temperature measurement methods and integrate this component into IGT systems where accurate delivery of thermal exposure is involved. This would allow real time monitoring of temperature distribution and monitoring of early biological effects of therapy. Control of the various forms of therapy may require modeling of the therapy response (which may be nonlinear), to ensure patient-specific local spatial control and control of the total therapy dose delivered. Novel methods for measurement of early biological effects of non-thermal therapies are necessary. For example, photodynamic therapy (PDT) is one local therapy that has been proposed, but it isn't clear what constitutes an early biologic marker of successful response to PDT.

IGT systems development. Optimization of IGT for the prostate requires several phases of technology development and pre-clinical evaluation as outlined in section 2.2. We anticipate that proposals will be received for two levels of effort. First, investigators who have IGT experience with totally integrated systems for another organ may seek support for the translation of research and development for an IGT system specifically for the prostate. Such applications may propose development of an integrated system within 2-3 years, with performance specifications and pre-clinical testing to be completed by the end of the grant period. Clinical trials would be performed after this grant period. Second, requests are anticipated for the development and integration of several, but not necessarily all, key components outlined in section 2.2, and for some evaluation of performance specifications or pre-clinical evaluation, where the IGT components are optimized for the scale of measurement and application to the prostate gland.

The R21/R33 mechanism is more suitable for technology development than other mechanisms previously available to the research community. It is also more suitable for promoting multi-disciplinary or bioengineering partnerships and in turn, industry partnerships. The R21 phase will address the feasibility of the integrated system or integrated components for one or more imaging modalities. If specific milestones are met, the research can progress to development and initial evaluation of the proposed IGT system. Alternatively, if the imaging technology or methodology is sufficiently mature for pre-clinical or clinical applications, the investigators can submit a R33 application, bypassing the R21 phase.

Industry has primarily focused on the development of navigational systems and specific imaging modality components of IGT for neurosurgery. At present, industry involvement in developing an integrated system for the prostate is very limited because they do not know which of the complex competing technologies is likely to develop into a significant market in the near term. Industry involvement with this initiative will therefore be strongly encouraged. The existing SBIR/STTR program already allows small businesses to focus on either development of an integrated system, by leveraging their experience

with IGT systems for other organs, or to develop one or more key components of an IGT system. If this RFA concept is approved, we will also propose a companion Program Announcement (no set-aside money) soliciting R41/R42 and R43/R44 applications under the STTR/SBIR programs.

Grant Program Approved For Statistical Modeling

The NCI Board of Scientific Advisors unanimously approved the Institute's plans to form a network of extramural researchers who would apply statistical modeling techniques to study the impact of cancer interventions on national cancer trends.

NCI plans to set aside $11 million over the next four years to fund six awards initially. Five more awards would be funded after two years.

Excerpts from the text of the concept statement follow:

Cancer Intervention and Surveillance Modeling Network (CISNET). Concept for a new RFA (cooperative agreement), six awards initially, five more awards after two years, estimated total cost $11 million. Program directors: Eric Feuer, phone 301-496-5029 or 301-496-8500, email: rf41u@nih.gov; and Martin Brown, phone 301-496-5716, email: mb53o@nih.gov

Modeling is the use of mathematical and statistical techniques within a logical framework to integrate and synthesize known biological, epidemiological, clinical, behavioral, genetic and economic information. Simulation and other modeling techniques have been utilized to describe the impact of cancer interventions (i.e. primary prevention, screening, and treatment) for hypothetical cohorts or in trial and other clinical settings. The goal of this concept is to promote the application and extension of these models to population-based settings in order to help answer "why" questions in the analysis of cancer trends. These questions are of importance to NCI because of the necessity of understanding: (1) if recommended interventions are having their expected population impact, and (2) to help predict the potential impact of new interventions on national trends. These studies will often involve extrapolation of controlled cancer intervention studies to estimates of U.S. population and community effectiveness. This type of modeling addresses issues of population based policies and programs, and is distinct from individual level models of risk and models of clinical decision making used at the individual patient-physician level. An additional goal of this concept is to advance methodology for modeling and to develop more uniform criteria for model validation in the population setting.

The proposed mechanism is a cooperative agreement that would support a Cancer Intervention and Surveillance Modeling Network. CISNET would consist of a network of grantees, organized by cancer site, with overall coordination and collaboration with NCI staff. This concept is based on the recommendations of the Surveillance Implementation Group Report which states that "statistical modeling and methods are needed to solve quantitative problems in cancer surveillance and to study the impact of cancer control interventions on the cancer burden. The report specifically endorses the CISNET proposal as "a good example of this latter type of research." The CISNET concept is also mentioned as part of the Prostate Cancer Five Year Research Plan (FY 1999-2003) recently submitted to the Subcommittee on Departments of Labor, Health, and Human Services, and Education and Related Agencies.

NCI has a long standing need to provide answers to critical research questions which cannot be obtained from direct observation because of expense, ethical, or other reasons. For example, a trial is only conducted in a limited study population under limited study conditions and extrapolation to other settings and conditions may only be feasible through modeling. Lead time, the time which a diagnosis is advanced through screening, often may only be estimated through modeling because it is unethical to leave a screen detected patient untreated until clinical symptoms develop NCI has supported a variety of small efforts in this area through in-house work, contracts and grants. The majority of extramural efforts have been directed at the analysis of specified cancer control interventions using a variety of modeling approaches, while the in-house work has mainly been directed toward addressing cancer surveillance issues at the national level. There has been growing recognition that much can be gained by integration of these two approaches.

Models increasingly have been used in recent years to inform public health policy decisions at the national level. In Europe, the cervical and breast cancer screening models developed by the MISCAN group have been used to design, monitor and evaluate national screening programs in several countries. Models have been used in the United States to help understand the implication of dramatic changes in national cancer statistics, such as patterns of increasing incidence related to screening in breast and prostate cancer, improving survival due to the dissemination of breakthrough treatment approaches in Hodgkin's Disease and Testicular cancer and the increase in juvenile brain cancer incidence which is at least partly related to the dissemination of CT detection technology.

Macro-level models use estimates of standard population-based statistics (i.e. birth rates, incidence, stage-distribution, relative survival, and mortality from causes other than cancer) as parameter estimates to model the life-process in terms of birth, the development of cancer, and death from cancer or other causes. The impact of cancer control interventions aimed at primary prevention, screening, and treatment are estimated by

changing the model parameters. This approach has proven useful in evaluating the potential costs and benefits of specific cancer control strategies, and exploring the impact of these interventions on population-based cancer incidence and mortality statistics. For example, CAN*TROL (a computer program developed by David Eddy for cancer control planning for the World Heath Organization and adapted for use at NCI) is a tool which has been used to examine the cost-effectiveness of various strategies for breast cancer screening, and models of this type are currently being used to evaluate the impact of the introduction of adjuvant therapy on breast cancer mortality as well as the impact of changes in modifiable risk factors on colon cancer incidence. CAN*TROL has proven to be an effective tool for responding to policy questions from Congress and other sources addressed to NCI.

Macro-level models have their limitations. For example, macro-level models do not capture individual disease history, especially the pre-clinical phase, and how early detection might alter that history. These dynamics are captured in models of specified cancer control interventions using microsimulation and other modeling techniques. While these modeling efforts have been invaluable in providing insight into the cost and effectiveness of specific intervention strategies, they are not designed to directly address the question of how trends in screening dissemination at the national level affect trends in cancer incidence, survival, mortality, and cost. Recent efforts have been made to adapt these models to address population level surveillance questions. While in the past these models have been utilized to model hypothetical cohorts in an organized screening program, the NCI has facilitated efforts to model opportunistic screening for multiple cohorts reflecting the varying cancer risk of U.S. population over time. For example current efforts are underway to model the impact of the dissemination of the PSA screening test in the US population on prostate cancer incidence and mortality. By validating against current population trends we can provide answers about lead time, overdiagnosis, and the timing and size of potential mortality declines.

In conjunction with the development of these models, there have been various methodologic spin-offs that have broad uses in a variety of modeling settings. For example, NCI researchers, in collaboration with extramural researchers, have investigated the issue of obtaining variability of estimates from microsimulations, estimation techniques have been developed for the incidence of pre-clinical prostate cancer from autopsy prevalence data, and issues related to model validation have been explored.

The purpose of this RFA concept is to enhance research on the development and use of models to evaluate the impact of cancer control interventions on population level statistics. NCI sponsored efforts to date in this area have been productive, yet modest in scope and exploratory in nature. Based on this experience, it seems clear that a more systematic approach will tap the potential of this area. To accomplish this, we propose an RFA cooperative agreement which will support a coordinated network of research activity in this area. Funding will consist of two rounds, two years apart, and in the first round applications will be restricted to three major cancer control sites where we have the most modeling experience, i.e. breast cancer, prostate cancer, and colorectal cancer. Depending upon our experience in the first round, the second round will include other cancers, especially tobacco control cancer sites. To keep applications focused, each will be limited to a single cancer site. While this cooperative agreement will be managed within the Cancer Surveillance Research Program (DCCPS), a technical advisory group consisting of representatives throughout NCI will be formed. The RFA will state that a somewhat balanced portfolio of grants across the three cancer sites will be a consideration in the funding plan.

Modeling efforts in the following areas are anticipated:

I. Dissemination patterns, e.g. modeling national patterns of the adoption and repeat use of mammography, PSA testing, etc. Data for such models are commonly obtained from national survey data and longitudinal case studies.

II. The impact of interventions on observed national trends. (A) Using estimates of the impact of interventions in controlled settings (e.g. meta-analysis of clinical trials or epidemiologic studies) and dissemination patterns. e.g., a model of the impact of adjuvant chemotherapy on colon cancer mortality starting in 1989; a model of the impact of changes in modifiable risk factors on colon cancer incidence from 1975 to 1995. (B) Using a model of disease natural history and operating characteristics of an intervention (validated against clinical trial and controlled observational experience) extrapolated to the population setting. e.g., model breast cancer screening trials and/or demonstration projects, and extrapolate the results to the U.S. screening experience. (C) Using discrepancies between modeled and observed population trends to study U.S. population and community effectiveness. e.g. study discrepancies between model predictions and observed data to better understand how community screening practices differ from trials (e.g. sensitivity of screening test may be better than in a trial because of improved technology, or worse because of less expert application of technology compared to the trial setting)

III. Predicting the impact of new interventions on national trends. e.g. model the impact of the preventative use of tamoxifen in high risk women on projected US trends in breast cancer incidence and mortality.

IV. Determining the impact of targeted cancer control interventions on population outcome, e.g. model the population impact of targeting different age groups, risk groups, adherence to initial versus repeat screening guidelines.

NIH Programs:

Advisory Panel On Alternative Medicine And Cancer Formed

NIH has chartered the Cancer Advisory Panel on Complementary and Alternative Medicine to advise the Institutes in the evaluation of complementary and alternative therapies for cancer treatment and prevention.

The CAPCAM is an initiative of the National Center for Complementary and Alternative Medicine (NCCAM) and NCI. The panel's key role is to serve in an advisory capacity to the NCCAM Director in the assessment of present and future CAM clinical trials and medical interventions, determine potential research opportunities, and develop a mechanism for communicating research results from these studies to key constituencies, NIH said in a statement.

"The formulation of this panel of experts represents a vital step toward rigorously evaluating the efficacy and safety of various CAM cancer therapies that demonstrate the potential for helping to reduce the burden of this disease," said William Harlan, acting director of the NCCAM.

The panel held its first meeting July 8-9.

Ernst Wynder, president and medical director of the American Health Foundation and clinical professor of community and preventive medicine at New York Medical College, will serve as chairman of the CAPCAM.

Other panel members are: June Brazil, clinical professional associate, Acupuncture & Oriental Medicine Program, Mercy College, Dobbs Ferry, NY; Peter Choyke, chief, MRI Diagnostic Radiology Department, Warren G. Magnuson Clinical Center, NIH; Ian Coulter, research professor and health consultant, RAND Corp., Santa Monica, CA; Susan Ellenberg, director, Division of Biostatistics and Epidemiology, FDA Center for Biology Evaluation and Research; William Fair, director, Prostate Diagnostic Center, Memorial Sloan-Kettering Cancer Center; James Gordon, director, Center for Mind-Body Medicine, Georgetown University School of Medicine; Michael Hawkins, Washington Cancer Institute, Washington, DC; David Hufford, professor, Medical Humanities, Behavioral Science, and Family Medicine, Pennsylvania State University College of Medicine, Hershey, PA; Frances Jacobs, clinical nurse coordinator, Rush-Presbyterian-St. Luke's Medical Center; Ralph Moss, director, The Moss Reports, Brooklyn, NY; Douglas Weed, chief, Preventive Oncology Branch, NCI Division of Cancer Prevention; Lauren Wood, senior clinical investigator, HIV & AIDS Malignancy Branch, NCI.

Ad hoc members of the panel include: Mitchell Hammer, International Communication Program & Peace and Conflict Resolution Program, American University; Edward Chapman, Newton, MA; Thomas Brown, M.D. Anderson Cancer Center. Ex-officio member: Jeffrey White, director, Office of Cancer Complementary and Alternative Medicine, NCI.

Funding Opportunities:

NCI Program Announcement

PAR-99-114: Review And Analysis Of Tobacco Industry Documents

Letter of Intent Receipt Date: Sept. 17, 1999; May 18, 2000

Application Receipt Date: Oct. 19, 1999; June 19, 2000

This PA is intended to stimulate research on a wide variety of scientific, technical, marketing, and tactical undertakings by the tobacco industry, which were documented in papers, memos, and other records. The systematic, comprehensive analysis and evaluation of these documents will greatly contribute to the understanding of what the tobacco industry knew and will help researchers and the public health community identify effective strategies to reduce tobacco use.

This PA will use the research project grant (R01) award mechanism. The total project period may not exceed four years. It is anticipated that applicants will request more than $250,000 direct costs per year. Therefore, modular grant application procedures will apply to this solicitation. Applicants requesting budgets greater than $500,000 in direct costs are required to contact program staff prior to submitting their applications.

Landmark tobacco litigation brought by the State Attorneys General and others, Congressional inquiries, and the Food and Drug Administration's historic investigation have resulted in the release of millions of previously inaccessible internal tobacco industry documents. Among other things, the documents contain information about the health consequences of tobacco use, cigarette design, tobacco marketing to particular demographic groups (including youth), the determinates of tobacco use, and how the industry has worked to undermine public health efforts that effectively reduce tobacco use.

The most comprehensive collection of documents is in Minneapolis, MN, at the State of Minnesota's Document Depository. This was established as part of the settlement reached in May 1998 to resolve the lawsuit brought by the Minnesota Attorney General and Blue Cross and Blue Shield of Minnesota against the tobacco companies. The depository contains an estimated 26 million pages of documents acquired through discovery in the Minnesota litigation and will, as a condition of the Minnesota settlement, incorporate documents released in any other smoking and health litigation in this country. Another 7 million pages of documents acquired through the litigation are stored in Guildford, England.

A rapidly increasing portion of the documents in the depository, as well as other documents, are now available through the Internet, at the following sites: the House of Representatives Commerce Committee site (http://www.house.gov/commerce/TobaccoDocs/documents.html); the Smokescreen site (http://209.8.58.18/); the University of California Library site (http://galen.library.ucsf.edu/tobacco/); the Tobacco Resolution (tobacco industry) site (http://www.tobaccoresolution.com/0002.htm); and the Blue Cross/Blue Shield of Minnesota site (http://www.mnbluecrosstobacco.com/toblit/trialnews/index.html). It is expected that additional sites will become available.

These newly released documents present a unique opportunity to make vast amounts of previously secret scientific information available in the fields of nicotine addiction, tobacco, marketing, and tobacco product engineering. The research findings contained in tobacco industry documents will only be useful if they undergo systematic analysis, and these analyses are published in the scientific and lay literature. Six analyses have already been published.

On July 17, 1998, the President issued an Executive Memorandum highlighting the importance of the tobacco industry documents that have been released as a result of recent tobacco litigation and congressional subpoenas. Citing the potential value of these documents to the public health community, the Memorandum directed the Secretary of Health and Human Services to do the following: (1) propose a method for coordinating review of the documents and making available an easily searchable index and/or digest of the reviewed documents; (2) propose a plan to disseminate widely the index and/or digest as well as the documents themselves, including expanded use of the Internet, and (3) provide a strategy for coordinating a broad public and private review and analysis of the documents to gain critical public health information.

The Program Announcement is one component of the Department's response to the President's directive. The Centers for Disease Control and Prevention is coordinating efforts to increase the availability of the documents through the Internet.

Specific Aims: Through the analysis of these documents, new information will be obtained about tobacco industry research, programs, and activities. Investigators may review the industry documents in order to assess the scientific validity and the application of the industry's findings. Information found in these documents can be analyzed in conjunction with the analysis of other data sets. This new information will help scientists understand tobacco use behavior and will guide health professionals in the development of new programs to reduce tobacco use.

The tobacco industry documents should be analyzed to gain scientific and technical knowledge in a number of areas, including, but not limited to the following: nicotine pharmacology; nicotine addiction; health consequences of tobacco use; tobacco product additives; tobacco product design and manufacturing; advertising and promotion; youth initiation; tobacco use cessation; disruption of scientific and public health programs; policy research.

Investigators will be faced with unique challenges in obtaining and analyzing these documents because of their large volume and limited organization. Investigators may choose to assess methods for retrieving and analyzing documents through electronic and other means.

All investigators funded under this program announcement will be asked to make the tobacco industry documents and indices they use available to scientists and lay audiences through the Internet. Investigators will be convened twice annually to discuss research methods and results of common interest.

Applications responding to the PAR should include two round trips for two-day meetings to Bethesda, MD, in the budget for each year.

Inquiries: Cathy Backinger, Division of Cancer Control and Population Sciences, NCI, Executive Plaza North, Room 241, MSC 7337, Bethesda, MD 20892-7337, phone 301-496-8584, fax 301-496-8675, email: cb270r@nih.gov

In Brief:

Radiation Therapy Pioneer Juan Del Regato, Dead At 90

(Continued from page 1)

Program. . . . **JUAN DEL REGATO**, a pioneer in radiation therapy, died on June 12 at age 90, of heart failure following abdominal surgery. He lived in Tampa, FL, where he taught at the University of South Florida College of Medicine and served as a consultant in radiation therapy at the James A. Haley VA Medical Center. **J. Frank Wilson**, one of del Regato's former students, now chairman of radiation oncology at the Medical College of Wisconsin in Milwaukee, said, "Few American physicians have had as great an impact on the development of a medical specialty as did Dr. del Regato. Throughout an extraordinary career spanning 60 years, he was a tireless and effective proponent for the advancement of radiation oncology." In 1949, del Regato founded the first training center in the U.S. dedicated to therapeutic radiology at the Penrose Cancer Hospital in Colorado Springs, CO. In the late 1960s, del Regato helped coordinate a clinical trial evaluating the effectiveness of radiation therapy in treating inoperable prostate cancer. He invented the "del Regato localizer," a device which facilitated the delivery of effective radiation treatments. He was an advisor to NCI when the National Cancer Act of 1971 was signed. He is also credited with founding the American Club of Therapeutic Radiologists, now called the American Society for Therapeutic Radiology and Oncology. "Up until the very end, Dr. del Regato showed a strong commitment to teaching the fundamentals of cancer to medical students. His passion for teaching was unequaled," said **James Cox**, one of del Regato's former students who is now head of radiation oncology at M.D. Anderson Cancer Center. Del Regato received numerous honors, including the Gold Medallion, Distinguished Service Award from the American Medical Association in 1993, the Gold Medal from ASTRO in 1977 and the Gold Medal from the American College of Radiology in 1968. He received the Bruninghaus Prize from the French Academy of Medicine in 1979, and he was one of only five U.S. radiation oncologists to receive the Beclere Medal from the Centre Antoine Beclere in Paris in 1980. He co-authored one of the first multidisciplinary textbooks, "Cancer: Diagnosis Treatment and Prognosis," and was recognized as a historian in the field of radiation therapy. Del Regato was born in 1909 in Camaguey, Cuba. He attended medical school at the University of Havana, which shut down at a time of political unrest. He finished medical school in Paris, studying at the Radium Institute and the Foundation Curie. Del Regato came to the U.S. in 1939. His wife of nearly 60 years, Inez, died earlier this year. He is survived by a son John del Regato, of Indianapolis, and daughters Ann Jaeger, of Lake Ann, MI, and Juanita Peters, of West Bloomfield, MI, five grandchildren and two great grandchildren. . . . **NORTHWESTERN MEMORIAL HOSPITAL** has received a $5 million gift allocated over five years from The Lynn Sage Cancer Research Foundation to fund innovative breast cancer research, patient care and education programs. The funds are earmarked to support innovative breast cancer research projects, digital mammography, physician recruitment, post-graduate fellowships, and expansion of staff and patient education programs. Northwestern Memorial Hospital is the primary teaching institution of the Robert Lurie Comprehensive Cancer Center of Northwestern University. . . . **WHITEHEAD FUNCTIONAL** Genomics Consortium, consisting of Millennium Pharmaceuticals Inc., Bristol-Myers Squibb Co., Affymetrix Inc., and the Whitehead Institute for Biomedical Research, has granted a royalty-free license to the SNP Consortium to use a key technology developed to discover single nucleotide polymorphisms. The SNP Consortium, a collaboration of 10 pharmaceutical companies and the Wellcome Trust, is funding the creation of a map of SNPs in the human genome. The Whitehead Consortium's technology is the subject of a pending patent application entitled "Pre-selection and Isolation of Single Nucleotide Polymorphisms" that claims a technology that is expected to enhance the efficiency of the SNP discovery process through a method called "reduced representation." In the reduced representation process, DNA from multiple sources is fragmented into subsets on the basis of size, thereby reducing the complexities associated with screening each set of DNA fragments for the presence of SNPs. "This technology is expected to significantly reduce the time needed and costs associated with creating a comprehensive SNP map," said **Eric Lander**, director of the Whitehead Institute Genome Center. "Accelerating the development of the SNP map will help lead to more effective methods for the diagnosis and treatment of genetically-based diseases."

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