THE CANCER LETTER

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BRCA 1 Mutation Finding Draws Attention To Potential Perils Of Genetic Testing

Last week's announcement of discovery of a genetic mutation associated with hereditary breast cancer among Ashkenazi Jews has given urgency to confronting the ethical, regulatory and logistical problems of conducting genetic testing in large populations.

Thus, the day after the triumphant announcement of discovery of a

(Continued to page 2)

In Brief

Discoveror Of H. Pylori Role In Ulcers Wins Lasker Foundation Clinical Research Award

SIX SCIENTISTS and a senator received awards from the Albert and Mary Lasker Foundation last week. **Barry Marshall**, Univ. of Virginia Medical Center, won the $25,000 Albert Lasker Clinical Research Award for his discovery that a bacterium, Helicobacter pylori, causes ulcers. Marshall's idea, announced in 1983, challenged half a century of belief that ulcers were caused by stress and too much stomach acid. "Enduring skepticism and derision for his unorthodox idea, Dr. Marshall nonetheless prevailed as researchers, bent on demolishing his hypothesis, ironically ended up confirming it," the foundation said. The Lasker award for basic medical research will be shared by five scientists, who will receive $10,000 each. Their work showed how T cells recognize invading organisms so that the immune system can be activated. The five scientists are **Peter Doherty**, St. Jude Children's Hospital; **Rolf Zinkernagel**, Institute of *Experimental Immunology*, Univ. of Zurich; **Emil Unanue**, Washington Univ. School of Medicine; **Jack Strominger**, Harvard Univ.; **Don Wiley**, Howard Hughes Medical Institute and Harvard. The $25,000 Lasker public service award was presented to **Sen. Mark Hatfield** (R-OR) for "outstanding leadership in support of biomedical research." This year was the 50th anniversary of the Lasker research awards. . . . **I. DAVID GOLDMAN**, director of the Massey Cancer Center, Virginia Commonwealth Univ., for the past seven years, has accepted a position as director of the Cancer Research Center at Albert Einstein College of Medicine in New York. **Francis Macrina** was named interim director of the Massey center, effective Sept. 15. Macrina has been associate director for basic research at the center since 1988. The university has appointed a search committee to recruit a permanent director. . . . **LANGDON MILLER**, a senior investigator in the NCI Cancer Therapy Evaluation Program, has accepted a position at the Upjohn Co., based in Kalamazzo, MI. Miller will become director of clinical oncology for Upjohn in the US.

Scientists, Insurers Disagree On Genetic Test Result Access

(Continued from page 1)

mutation on the BRCA1 gene, NCI Director Richard Klausner and National Center for Human Genome Research Director Francis Collins came to Capitol Hill to discuss the broad societal implications of the recent finding. (*A related story appears on page 4).*

Klausner, Collins and others brought together at a hearing of the Senate Cancer Coalition Sept. 29 described possible perils posed by genetic testing:

- Insurers are already using the results of genetic tests as a basis for denying health coverage. "Information on genetic susceptibility should be off the table for all health insurance companies," Collins said. However, preventing insurers from using genetic test results to deny coverage would require federal and state legislation.
- It is entirely possible that biotechnology companies' reference laboratories would rush to market tests that would present results, but offer little guidance. However, Collins and Klausner agreed that the industry should be given a chance to regulate itself as it launches genetic testing for cancer. "I think that if this goes bad, this bad experience is not going to be good for any of us," Klausner said. "So I am approaching this cautiously optimistically."

At this stage, with the knowledge of genetic testing for cancer susceptibility just starting to emerge, potential abuses of the information can be prevented, Collins said. "There is a wonderful opportunity here," he said. "It's probably a brief window of opportunity."

Health Insurance System "Unjust, Unworkable"

"Our current health insurance system is both unjust and unworkable," Collins said at the hearing. "It's unworkable because we all have mistakes in our DNA. And through the Human Genome Project we will find out what they are, and we will all become uninsurable.

"There is a moral argument as well," Collins said. "You don't get to pick your genes. None of us got to select what the DNA sequences are going to be. So they shouldn't be used against you. It seems to fly in the face of usual concepts of justice."

At this time, eight states prohibit insurers from using genetic susceptibility data in the valuation of risk. However, the problem is not limited to the 42 states that allow the use of such information, Collins said.

As it stands, about 40% of all health insurance in the US is provided by employers who are, in effect, self-insured and subject to federal regulation.

The problems with insurance should be given immediate attention, agreed Fran Visco, president of the National Breast Cancer Coalition and a member of the President's Cancer Panel.

"We've heard a great deal about insurance companies not wanting to cover experimental treatments," Visco said at the hearing. "We need to make certain that third-party payers cover participation in clinical trials. It makes economic sense and it makes social sense."

Visco said all genetic testing for cancer should be performed on protocol.

"We want to make certain that research protocols are available around the country, so all the families that want to participate can," Visco said.

Genetic Susceptibility Is A Factor In Underwriting

So far, the health insurance industry has taken a firm position: it considers genetic susceptibility information a vital part of the underwriting process.

"Private medical information, including genetic information, is vital to health insurance carriers," Harvie Raymond, assistant vice president of the Health Insurance Association of America, said at the hearing. "No company we know of is requiring genetic tests. Nor do we know of a company specifically asking for genetic test results... We are not currently using DNA-based genetic tests because the medical community is typically not using DNA-based genetic tests. When the medical community does begin using the tests, insurers will be at a disadvantage and at financial risk if they do not have access to the same

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information as applicants."

Raymond said insurance companies should not be denied access to the results of genetic tests to prevent "adverse selection," which occurs when a purchaser of insurance has more information than the underwriter.

"We believe that there should be access to that information, the same as any other relevant information," Raymond said.

"Why?" Sen. Dianne Feinstein (D-CA), asked incredulously.

"Because it has a bearing on the evaluation of the risk. We would also say that this information should be provided with true informed consent."

"No one would give consent," said Feinstein. "I mean, no one in the right mind."

Feinstein and Sen. Connie Mack (R-FL) are co-chairs of the coalition.

Beware Of Assay Bonanza

Klausner and Collins said that though cancer susceptibility testing has not become widespread, genetic testing for Huntington disease and cystic fibrosis has shown that the industry is capable of regulating itself.

"I think it would be a mistake to put in some kind of a heavy-handed oversight onto a field that is not quite developed, and slow it down," Collins said.

At last week's hearing, the genetic testing industry was represented by Elliott Hillback, president and CEO of Integrated Genetics Laboratories Inc. of Framingham, MA.

"If we can carefully put together a consortium-based, collaboration-based way to develop these new [cancer susceptibility] tests, we can begin to use them effectively very early in their life cycle, before every fact is known," Hillback said.

The industry has demonstrated restraint, commitment to quality as well as flexibility, Hillback said.

With the standards regulated by the College of American Pathologists and the American College of Medical Genetics, the industry has kept the HD test in research setting for about three years. At the same time, self-regulation has allowed for rapid updating of tests, with the CF assay being updated almost once a year, Hillback said.

"What scares the heck out of me is that we would get to some formal review process that would stop that progress," Hillback said. "It would be a shame to preclude the use of [cancer susceptibility] information early.

"I agree that we have to do this carefully. We and the other commercial laboratories that look at genetic testing have to think that way.

"We are in this for the long haul. Because there is no way we are going to get a financial return on our investment in this area in a one- or two- or three-year period," Hillback said.

Its past performance notwithstanding, the industry will be facing an entirely different set of challenges as it enters the cancer market, said Caryn Lerman, associate professor of medicine and psychiatry at the Lombardi Cancer Center at Georgetown Univ.

"Cancer is a much more prevalent disease [than CF and HD], and I think there will be much greater demand to provide this in clinical practice outside the research setting," said Lerman, a participant in the NIH Cancer Genetics Consortium.

Survey results Lerman presented in her testimony indicate that the market pressures for breast cancer susceptibility tests could be enormous:

- In one survey, 91% of women who had a mother, sister or daughter with breast cancer said they would want to be tested for susceptibility. The study was published in the American Journal of Medical Genetics (1995; 57:385-392). In another, ongoing study, in which BRCA1 testing was offered to members of families with a history of breast and ovarian cancer, 71% of individuals opted to receive their test results, Lerman said.
- At the same time, physicians, the likely target of pressure to order genetic tests, appear to have only a cursory understanding of genetics. In a recent test on genetics taken by 1000 primary care physicians, the average score was 73% [Academic Medicine, 1993; 68:625-639].

Thus, the pace of introduction of cancer susceptibility tests could outstrip the public's ability to interpret the tests, many observers warn.

"We need to be answering questions about whom we will eventually screen," Klausner said at the hearing.

"Will we be screening only individuals who were predetermined to be high-risk because they are members of particular high-risk families? Will we be screening subpopulations? Will we ever get to the point where it would be reasonable and effective to screen the entire population?

"What will we do with the information when a

change in cancer susceptibility is found? How will it help, not help, or even harm an individual who might receive that information? And, finally, how are we as a society dealing with the ethical, legal, social, insurance and psychological issues of the information that we are developing?" Klausner said.

The prospect of answering those questions in the midst of a gold rush generated by irresponsible purveyors of tests is worrisome, several observers warned.

"I must say that I am still worried whether this will work," Collins said of the plan to allow the genetic testing industry to regulate itself.

"Integrated Genetics is a very responsible company," Collins said. "But what is to prevent a much less responsible company from saying that they are going to make available the 'Jewish Breast Cancer Test' and market it extensively to general practitioners who may have very little information on how to use that information correctly, and scare the heck out of a very large number of people?

"Right now, I don't see that happening, but if it were to start to happen, then I think something more heavy-handed might be necessary," Collins said.

World's Highest Investing in Ethics Studies

In an attempt to anticipate the policy dilemmas, the National Center for Human Genome Research is spending 5% of its budget to fund grants on ethical research, an amount that constitutes the highest ever investment in ethics research, Collins said.

One product of this research was a set of recommendations for state and federal officials involved in the regulation of health insurance. The recommendations, developed last summer by working groups representing the genome project, the Department of Energy and the National Action Plan Against Breast Cancer, state:

1. "[Health] insurance providers should be prohibited from using genetic information or an individual's request for genetic services to deny or limit any coverage or establish eligibility, continuation, enrollment or contribution requirements.

2. "[Health] insurance providers should be prohibited from establishing different rates or premium payments based on genetic information, or an individual's request for genetic services.

3. "Insurance providers should be prohibited from requesting or requiring collection or disclosure of genetic information. Insurance providers and other holders of genetic information should be prohibited from releasing genetic information without prior written authorization of the individual. Written authorization should be required for each disclosure and include to whom the disclosure would be made."

A Poor Model: Sickle-Cell Anemia Tests

It is unclear how much government regulation would become necessary to make society benefit from genetic testing, Collins said.

"I am uncomfortable with the Big Brother attitude toward genetic testing, that it's not available because somebody thinks that it's not good for you," he said. "On the other hand, I think people are looking for guidance. To use a drug analogy, we don't have a system where people can walk up to the store and order chemotherapy because they think that maybe they have cancer, even though they have not been diagnosed."

Though genetic susceptibility testing is relatively young, it has had one dramatic failure: the programs that tested the African-American population for sickle-cell anemia in the 1970's.

"Very well intentioned programs in many states were put in place to offer, and in some cases mandate, sickle cell carrier testing for African Americans," Collins said.

Under those programs, people were tested without a clear explanation of what the test was about. Having received little or no counseling, many carriers concluded erroneously that they would inevitably develop the disease. Some of those carriers also lost their health insurance.

"I don't want to see that experience repeated," Collins said. "I think this technology is so powerful, so useful that we have a particularly strong obligation to do it right."

BRCA 1 Mutation Found In 1% Of Ashkenazi Jews

Nearly 1 percent of DNA samples taken from Ashkenazi Jews contained a specific mutation in the BRCA 1 gene, according to a study published last week.

The 185delAG mutation, found in both women and men of Eastern European Jewish descent, may predispose its carriers to breast, ovarian, colon or prostate cancer.

The study, published in the October 1995 Nature Genetics, offers the first evidence that an alteration in the BRCA 1 gene is present at measurable levels not only in families at high risk for breast cancer, but in a subset of the general population.

"This study raises the feasibility of testing for predisposition to cancer in a defined population," NCI Director Richard Klausner said. "We do not know whether individuals with the mutation indeed carry an increased risk of cancer."

Klausner said the Institute would begin a clinical study later this month to try to quantify the risk the mutation carries. The study would enroll about 5,000 Ashkenazi Jews living in the Washington, DC, area. Participants would be screened for the mutation and interviewed about their family medical history, but would not learn their DNA test results.

Widespread Testing Not Recommended

There are an estimated 7 million Ashkenazi Jews living in the US. About 70,000 of them, or 1 percent, are likely to carry the mutation, Francis Collins, director of the National Center for Human Genome Research and a co-author on the study, said.

Collins and the other authors said the data were too preliminary to recommend widespread testing for the mutation.

"While the finding raises the possibility of testing, it does not provide any data on precise cancer risk," Jeff Struewing, an investigator in the NCI Genetic Epidemiology Branch and an author of the paper. "Until more detailed information is available, it is premature to recommend that Ashkenazi women seek BRCA 1 testing."

BRCA 1 was isolated one year ago. When one of its two copies is inherited in an altered form, the gene predisposes women to breast or ovarian cancer. In men, it may increase the risk of prostate or colon cancer.

The BRCA 1 gene has been found to have a large number of different alterations. Women who inherit a BRCA 1 mutation are estimated to have up to a 90 percent lifetime chance of developing breast cancer, and an 84 percent chance of developing ovarian cancer. Because these data are based on studies of families with strong histories of cancer, scientists have not been able to determine the risk of cancer linked to BRCA 1 in women without a strong family history of the disease.

Over the past year, two research teams independently observed a specific, two-base deletion in the BRCA 1 genes of 10 families with histories of breast and ovarian cancer. The scientists noticed that each of the families was of Ashkenazi Jewish origin.

Following up on these studies, three research groups in the US and Israel jointly tested 858 DNA samples from unrelated Ashkenazi Jews. The participants were randomly selected regardless of family history of cancer.

Eight of the samples contained one copy of the BRCA 1 gene that had the 185delAG deletion. This carrier rate, 0.9 percent, is three to five times higher than the estimated carrier rate for all BRCA 1 mutations combined in the general US population.

The researchers also tested 815 DNA samples from individuals not selected for ethnic origin. None had the mutation.

The mutation might account for as much as 16 percent of breast cancer and 39 percent of ovarian cancer in Ashkenazi Jewish women age 50 and under, the scientists said. That estimate is based on US census and epidemiological data, and data on BRCA 1-linked cancer. In the general US population, inherited BRCA 1 alterations are estimated to contribute to 4 percent of breast cancer and 12 percent of ovarian cancer.

Besides Struewing and Collins, other authors of the paper were Dvorah Abeliovich, Tamar Peretz and Naaman Avishai of Hebrew Univ. in Jerusalem, Michael Kaback of Univ. of California, San Diego, and Lawrence Brody, of the National Center for Human Genome Research.

Further Studies Planned

NCI is working with leaders of the Washington-area Jewish community to design the clinical study, expected to begin later this month, Klausner said. Preliminary results may be available by next March, he said.

Participants in the study would be asked for a few drops of blood, which would be tested for the mutation. Some of the participants would be volunteers, while others would be selected randomly through telephone calls.

Individuals results would not be revealed to the participants in this phase of the study, NCI said. "Genetic testing and counseling may be available once more is known about the effects of this particular alteration in the BRCA 1 gene," the Institute said in a statement.

Margaret Tucker, chief of the NCI Genetic Epidemiology Branch, will lead the clinical study.

NCI also is planning a study on Long Island, NY, and will expand and initiate other studies at centers around the US, Klausner said.

Patricia Barr, a lawyer and member of the National Breast Cancer Coalition, said the prospect of testing for a predisposition to breast cancer poses profound ethical questions.

"In my judgment, the results of the study are not cause for Ashkenazi Jewish women to seek private breast cancer genetic testing," Barr said. "We simply don't know what a positive result for this mutation would mean. We do not know about the timing or frequency of disease, and furthermore, we don't know what to advise women about treatment."

More basic and clinical research is needed to answer questions about BRCA 1, Barr said. "We must press to expand research funding so that these findings can be followed up with clinical trials," she said.

BMS Oncology And R&D Units Shift Senior Management

Donald Hayden, president of the Bristol-Myers Squibb Oncology/Immunology Division, was promoted to senior vice president, worldwide franchise management and business development at Bristol-Myers Squibb Co. of Princeton, NJ.

Hayden will be replaced by Michael Loberg, whose most recent position was as senior vice president, US Pharmaceuticals at BMS.

Loberg joined Squibb in 1979 as director of radiopharmaceutical research and development.

In other personnel changes:

- Stephen Carter, senior vice president of the Bristol-Myers Squibb Pharmaceutical Group, has accepted a job as senior vice president, research and development, at Boehringer Ingelheim Pharmaceuticals Inc. of Richfield, CT. Carter begins the new job next week.

A spokesman for BMS said no successor to Carter has been appointed.

- Sol Rajfer was named senior vice president, worldwide clinical research and development at the BMS Pharmaceutical Research Institute. Rajfer is the former vice president, cardiovascular clinical research, at the research institute.
- Andrew Bodnar, formerly president of oncology, immunology and worldwide strategic business development at BMS, was named vice president, medical and legal affairs.

Earlier this year, BMS combined its oncology and immunology businesses.

The latest changes come at a pivotal time for the BMS oncology business, several observers said.

The long-time leader in cytotoxic drugs reported $1.34 billion in worldwide sales of oncology products in 1994, industry analysts said.

However, the recent merger of Pharmacia AB of Stockholm and the Upjohn Co. of Kalamazoo, MI, has created a strong No. 2 oncology company with the combined sales of about $700 million.

On another front, manufacturers of generic drugs are preparing to cut into the sales of the BMS drug Taxol, and another rival, Rhone-Poulenc Rorer of Paris and Collegeville, PA, is preparing for a second attempt to receive US approval for the drug Taxotere, a Taxol analog.

The FDA Oncologic Drugs Advisory Committee is scheduled to hear RPR's presentation on Taxotere on Oct. 17.

ASCO Seeks Applicants For Young Investigator Award, Career Development Award

American Society of Clinical Oncology is seeking applicants for its Young Investigator Award and Clinical Research Career Development Award.

The Young Investigator Award is a one-year grant of $32,500 as seed funding to encourage quality research in clinical oncology, both basic and applied. Individuals who have previously been a principal investigator on a grant or received a career development award are not eligible.

The Clinical Research Career Development Award is a three-year grant of $50,000 per year plus 5% to cover travel and other indirect costs. The total project award over three years is $157,500.

The CDA is designed for individuals who have made their initial commitment to clinical research in their first full-time academic position. The award provides support and protected time needed to establish an independent cancer research program competitive for national funding.

Application deadline for either award is Nov. 15. To request an application packet, contact the ASCO Chicago office, tel: 312/644-0828.

Two US Cancer Centers Receive Large Donations

Cancer centers at two US universities this week received unusually large donations from successful businessmen who said they are committed to improving people's lives.

An industrialist who lost his parents to cancer donated $100 million to the Univ. of Utah in the largest single financial contribution ever to medical research from an individual.

A financial information company founder gave Johns Hopkins Univ. $55 million, part of which will support a new building for the Johns Hopkins Oncology Center.

The unrelated gifts come at a time when cancer centers are searching for strategies to maintain research budgets traditionally supported by federal grants and patient care income.

Genetics Research Is Huntsman Priority

The $100 million donation to Utah, which is to be made available over the next five to 10 years, is equivalent to the annual budget for NCI's cancer centers core grant program.

Jon Huntsman Sr., 58, founder of four chemical and packaging businesses known collectively as the Huntsman companies, announced his family's donation Oct. 2 at a groundbreaking ceremony for a $50 million building that will house the Huntsman Cancer Institute at Univ. of Utah.

Huntsman said he made a commitment after his mother's death from breast cancer 30 years ago to fight cancer, but never thought he would be in a financial position to make a difference. His father died of prostate cancer. Huntsman was diagnosed with prostate cancer and mouth cancer three years ago.

The privately held Huntsman companies, which include Huntsman Chemical Corp. and Huntsman Corp. (formerly Texaco Chemical Co.) anticipate 1995 sales revenues of $4.3 billion.

"Our family's commitment is to help find a cure for cancer," Huntsman said. "Now more than any other time in history, there is new hope for a cure for this anguishing and ruthless disease."

The Huntsman Cancer Institute was established in 1993 with a $10 million pledge from the Huntsman family. Donations gathered by Huntsman will add an additional $51 million to the total the family pledged this week.

Other contributions to the cancer center include $15 million from the British pharmaceutical firm Glaxo-Wellcome and $10 million from the Primary Children's Foundation. Other major contributors were Kerry Packer, a friend of Huntsman and chairman of Australia's Consolidated Press Holdings Corp., the state of Utah and the Church of Jesus Christ of Latter-Day Saints.

The funds will be used to build a research and treatment center and to recruit about 50 senior researchers, said Raymond White, director of the institute.

The Institute will focus primarily on human genetics. Last year, the university received international attention from the discovery of the BRCA 1 gene, found by a research team led by Utah's Mark Skolnick.

Huntsman and university officials said the institute will make use of the genetic histories available at the Mormon church's genealogical library in Salt Lake City.

"Cancer is an insidious disease which impacts the life of one in every three people," Huntsman said. "The medical establishment's battle to stem this plague has been waged for many years with little success. We feel that by combining internationally recognized scientists with a first-rate medical school, along with generations of genealogical records kept in Utah, the opportunity for a significant breakthrough never has been better. Cancer will be defeated."

Bloomberg's Pledge To Hopkins

Michael Bloomberg, founder of Bloomberg Financial Markets, a New York-based financial information company, said his $55 million gift to Hopkins is to be divided among the university's eight schools and library. Some of the money will go toward a cancer treatment center and a cancer research building. Part will go toward increasing the school's endowment. The rest will go toward capital projects, such as renovating the library and constructing campus buildings.

"I'm personally improving the world and people's lives with my gift," said Bloomberg, a 1964 graduate of Hopkins. "What better thing could I do? How better can I repay society for all the opportunities I've had?"

Bloomberg is the chair-elect of the university's board of trustees. He previously gave the university $8 million, which went in part toward constructing the Bloomberg Center for Physics and Astronomy.

Rush-Presbyterian Professor Found Guilty Of Misconduct

The HHS Office of Research Integrity has made final findings of scientific misconduct in the following case:

Alan L. Landay, Rush-Presbyterian-St. Luke's Medical Center: Based on an investigation conducted by the institution, ORI found that Landay, an associate professor, Dept. of Immunology/Microbiology, engaged in scientific misconduct involving two instances of plagiarism in publications related to two Public Health Service grants. Landay has entered into a Voluntary Settlement Agreement with ORI in which he has accepted ORI's finding and, for a two-year period has voluntarily agreed to: exclude himself from serving in any advisory capacity to PHS, and certify in every PHS research application or report that all contributors to the application or report are properly cited or otherwise acknowledged.

ORI acknowledged that Landay cooperated with the institutional investigation and the ORI review, accepted responsibility for his actions, and appropriately corrected the scientific literature.

The two published papers (Coon, J.S., Landay, A.L., & Weinstein, R.S. "Advances in flow cytometry for diagnostic pathology." Laboratory Investigations 57:453-479, 1987; and Landay, A., Hennings, C., Forman, M., & Raynor, R. "Whole blood method for simultaneous detection of surface and cytoplasmic antigens by flow cytometry." Cytometry 14:433-440, 1993) that contained plagiarized text have been corrected (Landay, A. Correspondence. Laboratory *Investigations 70:134, 1994*; and Landay, A., Jennings, C., Forman, M., & Raynor, R. Correction. Cytometry 14:698, 1993).

RFA Available

RFA CA-95-021

Title: **Specialized Programs Of Research Excellence In Gastrointestinal Cancer**

Letter of Intent Receipt Date: Dec. 4

Application Receipt Date: Feb. 14

The Organ Systems Coordinating Branch of the NCI Div. of Cancer Treatment, Diagnosis and Centers (DCTDC) invites applications for center grants (P50) for Specialized Programs of Research Excellence (SPORE) that address Gastrointestinal (GI) Cancers of highest incidence and mortality, i.e., colorectal and/or pancreatic cancers.

The intent of this initiative is to recompete the SPORE in GI Cancer and to expand the program with the addition of at least one new SPORE through open recompetition.

Awards will be made to those institutions at which the highest quality balanced translational research approaches on the prevention, etiology, screening, diagnosis, and treatment of colorectal and/or pancreatic cancers can be conducted.

Because basic research in pancreatic cancer has lagged behind that of the other major solid tumors, greater leeway is given for basic research studies on pancreatic cancer. However, such studies must have translational potential or significance.

SPOREs are at institutions that have made or will make a strong institutional commitment to the organization and conduct of these programs. SPORE applicants will be judged on their current and potential ability to translate basic research findings into innovative research settings involving patients and populations. Each SPORE is encouraged to conduct rehabilitation and quality-of-life research.

Each SPORE must provide career development opportunities for new and established investigators who wish to pursue active research careers in translational GI cancer research; develop and maintain human GI cancer tissue resources that will benefit translational research; develop extended collaborations in critical areas of research need with laboratory scientists and clinical scientists within the institution and in other institutions; and participate with other SPORES on a regular basis to share positive and negative information, assess scientific progress in the field, identify new research opportunities, and promote inter-SPORE collaborations to resolve areas of scientific controversy.

Each SPORE and the "network" of SPOREs is expected to conduct research that will have the most immediate impact possible on reducing incidence and mortality to human GI cancer.

Each SPORE should support a mix of basic and clinical researchers whose formal interactive and collaborative research efforts will result in new approaches for early detection, diagnosis, therapy, prevention, and control. The SPORE mechanism is not intended to support basic research to the exclusion of clinical research or vice versa.

NCI anticipates making one and possibly two awards, and anticipates setting aside $3 million total for the initial year's funding.

Inquiries: The RFA may be obtained electronically through the NIH Grant Line (data line 301-402-2221) and the NIH GOPHER (gopher.nih.gov) and by mail and e-mail from: Andrew Chiarodo, DCTDC, NCI, Executive Plaza North Suite 512, Bethesda, MD 20892, tel: 301/496-8528, fax: 301/402-0181, e-mail: chiaroda@dcbdcep1.nci.nih.gov