

THE WHITE HOUSE
WASHINGTON

September 18, 1996

MEMORANDUM FOR: CAROL RASCO
BRUCE REED
DON BAER
DOUG SOSNIK
ALEXIS HERMAN
KAREN HANCOX
BILL CURRY

FROM: Elizabeth Drye
Debbie Fine

SUBJECT: Proposal for POTUS to Visit Cancer Center

This year marks the 25th Anniversary of the National Cancer Act, which gave the National Cancer Institute a mandate to pursue new scientific leads in research and apply the results to improve methods of cancer detection, treatment, prevention and control.

Several groups in the private sector have formed a coalition to raise public awareness about the importance of cancer research in honor of this Anniversary. This coalition and the National Cancer Institute have both approached us to request a Presidential event commemorating the Act's 25th anniversary in the next couple of months. Tony Podesta has been representing the private sector coalition, which consists of the American Cancer Society, National Breast Cancer Coalition, American Nurses Association, survivors, researchers and others.

Below for your consideration is a potential Presidential event on the road or in DC in the near future. If you think it's worth pursuing, we will draft a formal scheduling proposal. We would like to get back to Tony Podesta by next week if possible with a sense of whether or not this is a possibility.

SUGGESTED PROPOSAL

1. The President could visit one of the major cancer centers, which are located all over the country. There he could make remarks to patients, researchers, cancer center employees, and cancer survivors on his accomplishments and agenda for the future. Prior to remarks, the President could also tour the facility and/or sign the National Coalition of Cancer Survivors' "Ribbon of Hope." (The

"Ribbon of Hope" is similar to the AIDS quilt in its symbolism; it travels all over the country for people to sign as an expression of hope and concern. At the outset of its tour approximately one year ago, the First Lady signed it. It is due to be put on display in Albuquerque at the annual meeting of the National Coalition of Cancer Survivors October 4-6.)

2. Podesta also suggested the President deliver remarks at the Nina Hyde Breast Cancer dinner on the evening of September 24th in Washington D.C.

SUGGESTED MESSAGE

- In the 25 years since passage of the Cancer Control Act, we have made dramatic gains. Death rates from children's cancers have declined by almost two-thirds. Today, 10 million Americans owe their lives directly to cancer research.
- But cancer still kills one out of every five Americans. This year nearly 1.4 million people in the U.S. will be diagnosed with cancer, and more than 550,000 people will die of cancer--more than 1,500 people a day. Research offers tremendous promise to improve survival rates.
- President Clinton has a strong record of support for cancer research and other cancer initiatives. Review record of accomplishment, specifically touching on FDA's cancer initiative, breast cancer research, the tobacco initiative (smoking is the cause of over 30% of cancer deaths), etc.
- Under President Clinton's leadership, the Administration is continuing to build on that record with several initiatives that will help us as we move into the 21st century. See attached for specific potential announcements of NCI activities.

COURSE OF ACTION

1. Would you support consideration of an event commemorating the 25th Anniversary of the Cancer Control Act?

_____ **YES**

_____ **NO**

cc: Jennifer Klein ✓
Barbara Woolley

POTENTIAL CANCER INITIATIVES FOR POTUS TO HIGHLIGHT/ANNOUNCE

NCI has initiatives underway to:

1. **Identify the keys to each cancer.** NCI's **Cancer Genome Anatomy Project** will speed cancer detection and improve treatment by helping doctors quickly identify specific cancer genes within tumors. Under the project, NCI is building a complete index of genes expressed as tumors and is investing in developing technologies that can identify these genes in minutes.

Status: NCI has announced to scientific community.

2. **Speed the approval and use of new treatments.** NCI's **Informatics Initiative** will link NCI, the FDA, and public and private research centers throughout the nation to provide instant access to the latest data and support FDA's new drug approval process.

Status: NCI has not formally announced; known to scientific community.

3. **Develop novel, targeted drug therapies.** NCI is supporting the development of cancer cell-specific viruses and other novel therapies that carefully target cancer cells and better spare healthy cells.

Status: NCI has not formally announced; known to scientific community.

4. **Expand veterans' access to clinical trials of cutting-edge therapies.** NCI has crafted an agreement with the VA to increase veterans' participation in and speed completion of clinical trials. NCI announced a similar arrangement for DoD beneficiaries earlier this year. NCI will work to bring private insurers into the initiative.

Status: VA agreement is ready and has not been announced.

5. **Build collaboration.** NCI has catalyzed and will help underwrite the creation of the National Cancer Policy Board. Modeled on the National Academy of Sciences, the board will bring together many sectors of society -- including business, government, doctors, and advocacy groups -- to debate cancer policy issues affecting the nation (e.g. tobacco control and regulation of environmental toxins).

Status: NCI has announced to scientific community.

PODESTA

associates, inc.

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FACSIMILE TRANSMISSION

TO: JENNIFER KLEIN

FAX #: 456-7028 CODE: 202

DATE & TIME: 9/12, 2:30

FROM: REID DETCHON / TONY PODESTA

NUMBER OF PAGES INCLUDING COVER SHEET: 2

MESSAGE

IF A PROBLEM OCCURS WITH THIS TRANSMISSION, PLEASE CALL (202)393-1010.



Memo

Date: September 12, 1996

To: Jennifer Klein

From: Tony Podesta

Subject: Cancer Research Event for the President

Here's a shorter summary of our scheduling request:

WHAT IT WOULD LOOK LIKE: Pictures of the President visiting patients and/or researchers in federally funded trials of new cancer treatments, and/or signing the National Coalition of Cancer Survivors' "Ribbon of Hope," **followed by** remarks to an audience of researchers, cancer center employees, patients, and cancer survivors who have benefited from the results of research.

WHERE IT WOULD BE: Major cancer centers throughout the country are eager to host the President. We'd love to have him in Philadelphia. Other attractive locations include Georgetown and Yale and these cities: Los Angeles, Miami, Detroit, New York, Houston, Tucson, AZ, and Columbus, OH.

WHAT HE WOULD SAY: Cancer research is the kind of program all Americans want the government to support, but **its future may be jeopardized by Republican budget cuts if the Dole tax plan is enacted.**

In the 25 years since President Nixon declared war on cancer, we have made some dramatic gains. Death rates from children's cancers have declined by almost two-thirds. But we haven't "cured" cancer. Research offers that promise.

New research has begun to identify the genetic keys to the disease. Now the National Cancer Institute (part of NIH) is launching a project that will enable doctors to identify the specific cancer genes within tumors and to target their treatment accordingly. Breakthroughs like these depend on continued support of research.

WHY HE SHOULD DO IT: Cancer kills one out of every five Americans. Every voter knows someone who has cancer -- usually in their own family. The President has a strong record of support for cancer research and other cancer initiatives. This issue, on the 25th anniversary of the National Cancer Act, provides another chance to dramatize the risk of electing Bob Dole and his team of budget cutters.

NATIONAL
CANCER
INSTITUTE

Fax Transmittal

Office of Cancer Communications
Office of the Associate Director

Building 31, Room 10A31
Bethesda, Maryland 20892

301-496-6631
Fax 301-402-4945

Date 9/11/96
To Elizabeth Dye
Fax Number 202-456-7028 7431
From Dr. Klausner
Cover Sheet plus 3 Pages Transmitted

Message

As discussed.NCI's statement.

A BRIDGE TO THE FUTURE OF CANCER TREATMENT

IMPACT OF CANCER ON SOCIETY

- More than any other disease, Americans fear cancer, a term that encompasses more than 100 different diseases. This year nearly 1.4 million people in the United States will be diagnosed with cancer, and more than 550,000 people will die of cancer--more than 1,500 people a day. One of every five deaths in the United States is from cancer.
- Twenty-five years ago, the United States declared war on cancer and enacted the National Cancer Act of 1971. It was clear then that cancer would not go away by itself, and that its terrible human toll could only get worse without a concerted national effort to control the disease.

IMPACT OF RESEARCH ON CANCER

- Since 1971, scientists have discovered the causes of many cancers and they have proven that cancer can be curable. Today, more than 10 million of our family members, friends, neighbors, and coworkers owe their lives to cancer research. And seven million of them are long-term survivors.
- Cancer survivors are alive today because 25 years of research in prevention, diagnosis, and treatment methods have given doctors better information and tools to deal with the diseases.
- America's youth have received the most benefit from this country's investment in cancer research. Scientists have been instrumental in developing better treatments. Thanks to the hard work and vision of these individuals, most cases of childhood leukemia are now curable. Death rates from children's cancers have declined by more than 62 percent. This was only a dream 25 years ago.
- Cancer research also made possible dramatic improvements in the survival rate of adults. The death rate for testicular cancer, for example, has declined 66 percent and now has a five-year survival rate of 95 percent. And Hodgkin's disease, which can strike young adults in the prime of their lives, was once one of the most feared cancers. Today, the majority of Hodgkin's disease patients can be successfully treated, and most of them are cured. The cancer death rates are falling for major cancers such as colon and rectum cancers, breast cancer, pancreas cancer, leukemia, stomach cancer, ovarian cancer, and cancer of the uterus.
- But most importantly for the future, research has identified the genes that make cancers grow, and the genes that prevent the growth of cancer cells. All of this new information provides a bridge to the 21st century.

LOOKING FORWARD TO THE 21ST CENTURY

Now, we begin to look forward to the 21st century, assured that the research of the 20th century is laying a solid foundation for our future. We can look forward to:

- **New technologies.** The National Cancer Institute is beginning a new initiative to allow us to finally know the nature of each cancer. If we know what a cancer is we can stop it before it starts. This initiative, called the Cancer Genome Anatomy Project, could lead to a new generation of diagnostic tools for all tumor types. It could lead to revolutionary approaches to early detection, accurate diagnosis, and appropriate choice of treatment for each type of cancer. If successful, this initiative could transform the practice of oncology and accelerate research on what causes cancer. The initiative will have two major thrusts. First, it will support the development of technologies that will enable high-speed analysis of genes and their products within any cell. Second, it will build a complete index of all genes that are expressed in tumors. This new initiative is possible because of the tremendous gains in knowledge of the past 25 years about why a cell divides or dies or becomes a cancer. By identifying every gene that contributes to cancer, and coupling this knowledge with the new technology, we will be able to determine the fingerprint of a tumor in just minutes. Through this initiative, the National Cancer Institute is building a bridge to the medicine of our future, a future that will let the doctor examine the tumor's fingerprint in much the same way that a detective studies the fingerprints and other evidence left at the scene of crime. Laboratory tests of the future will examine the fingerprint of the cancer, to see which genes, gene products, and interactions within the cell have led to the development of a cancer. With this knowledge, doctors will help patients select treatments designed to act against the character of a particular tumor. [Note: This initiative has not been announced outside of the scientific community.]
- **Better treatments.** The National Cancer Institute has undertaken two major initiatives to bring better cancer treatments to the people. The first, an Informatics Initiative, will create an information system that links the NCI, the Food and Drug Administration, pharmaceutical companies conducting new cancer treatment studies, all of the nation's cancer centers, and the thousands of hospitals and the nearly 10,000 doctors participating in cancer research into one information system. This Informatics system will speed up research by enhancing the consistency of study results across the country, provide instant access to the latest data, and support FDA's new drug approval process. This Informatics Initiative will also make information about the prevention, detection, and treatment of cancer available to all. It will link to computerized systems of NCI that describe in consumer-friendly language all cancer treatment studies under way, and provide detailed information for physicians on cancer studies as well as the latest standard treatment options for all cancers. The second, an Initiative to Develop Novel Drug Therapies, will capitalize on recent research advances to develop better treatments. Imagine a

virus that only grows in cancer cells. This virus would infect and kill tumor cells without harming normal cells. These and other creative potential cancer treatments have names like immunotoxins, antisense technologies, and oncolytic viruses. Science fiction? These approaches for the 21st century are already being studied in clinical research supported by the National Cancer Institute, and specifically target only a patient's cancer cells. This is in contrast to today's cancer treatments, which are like shotgun blasts, catching healthy cells in the crossfire. This fact accounts for the side effects of many cancer therapies. New drugs are already being tested in cancer patients. [Note: Neither of these initiatives has been publicly announced. Both are known in the scientific community.]

- **Greater Access To the Benefits of Research.** Cancer patients want access to the best, newest treatments available. As a result, the National Cancer Institute has established a model initiative that will give patients in managed care systems that kind of access. The initiative began with the Department of Defense, to refer military families into medical studies when that is the appropriate treatment choice for patients. Another agreement, with the Veterans Administration, will strengthen the information and treatment choices for patients who are veterans. The NCI will work to bring other private managed care systems under the initiative, and help bring the discoveries of medical research to all. [Note: The DOD initiative was announced earlier this year, but received coverage only in the trade press. The VA agreement could be signed and announced in October.]

- **Society Working Together.** The National Cancer Institute has spearheaded partnerships within all segments of our society to address the cancer problem and make the discoveries available to everyone. People from all sectors of society--teachers, businesses, government, scientists, doctors, nurses, patients, and advocacy organizations--will work together to confront issues like tobacco control, cancer care, government regulations that control environmental toxins, and many other societal issues. They will be brought together under a new initiative proposed and supported by the National Cancer Institute and carried out by the National Academy of Sciences. This initiative, known as the National Cancer Policy Board, will provide a forum where individuals from the diverse participants in the nation's cancer effort can debate policy and make recommendations for cancer policy affecting the nation. This Board will go beyond research and look at societal issues such as smoking control, and the conduct of cancer treatment studies in managed care settings. [Note: This initiative has been announced in the scientific community, but not to the public.]

June 6, 1996 ✓

MEMORANDUM FOR ELIZABETH DRYE, JEN KLEIN, BARBARA WOOLLEY

FROM: Debbie Fine

SUBJECT: Meeting on National Cancer Act

I. LOGISTICS

DATE: Monday, June 10, 1996

TIME: 3:00pm to 4:00pm

LOCATION: Room 472 OEOB

II. PURPOSE

The primary purpose of this meeting is to listen to ideas about how the Administration, specifically the White House, can commemorate the 25th Anniversary of the National Cancer Act. Currently there are two tracks on this issue: (1) National Cancer Institute (NCI)/government activities; and (2) private sector activities. The private sector effort is forming a 501(c)3 to drive a public education campaign on the importance of cancer research. This coalition includes American Cancer Society, National Breast Cancer Coalition, American Nurses Association, survivors, researchers, and others. The private and public sector efforts work very closely together (Ellen Sigal is on the Advisory Board of NCI), but they established an independent effort so that their activities are not restricted.

Elizabeth and Jen have met with Dr. Klausner of NCI previously to hear about some of his ideas, and I have spent time on the phone with Ellen Sigal from the private sector. We have all stressed that we want to hear more about what they are planning in order to see how we might plug in, and that we do not want anything to revolve around our participation. Ideas have ranged from announcing a 25 year strategy to having the President appear in a psa.

III. PARTICIPANTS

White House

Elizabeth Drye

Debbie Fine

Jen Klein

Barbara Woolley

HHS

Richard Klausner; Director of National Cancer Institute

Victor Zonana; Deputy Assistant Secretary for Public Affairs at HHS

Private Sector

Tony Podesta; Chair of Podesta and Associates

Ellen Sigal; she runs a consulting company that focuses on environmental and construction issues. She became involved in cancer and biomedical research when her sister died of breast cancer years ago. She is the Chair of the Board of the Cancer Institute at Duke and the head of the budget committee for the National Cancer Institute Advisory Board.

IV. ATTACHMENTS

I have attached, 'fyi, some excerpts from NCI's draft bypass budget proposal for you to review prior to meeting for background on the issue if you are interested.

Foreword

"A world without science is a world without hope"

—PETER MEDAWAR

Both wonder and heartache. The wonder has come both from our success in treating certain tumors and from our astonishing new knowledge of how cancer cells work. These advances have been heartening, and they herald great promise for the future. The heartache comes from what we haven't been able to do. Our understanding of cancer's complexities remains incomplete, frustrating our fervent desire to eradicate this scourge once and for all. During 25 years of tireless and exacting sciences since passage of the National Cancer Act, we have made great strides against cancer, but there is still much to learn, much to do.

Over 40 percent of us will develop cancer; over 20 percent of us will die from cancer. Within five years cancer will be the leading cause of death in the United States, responsible for over 6 million years of life prematurely lost each year and an annual cost to the economy of over \$100 billion.

How do we continue to move forward? Part of the answer is to sustain proven research programs that have brought us to this juncture. At the same time, we must recognize and seize the extraordinary opportunities for further progress earned through our national investment and our diligence. We have built a successful discovery process, attracted some of the best

scientific minds to the cancer problem, and initiated ground-breaking programs that already have yielded critical knowledge, improved patient care, and saved lives. We must continue to support these endeavors, ensuring that they remain vital and productive.

The Congress has requested that the Director of the National Cancer Institute (NCI) prepare a budget estimate for cancer research.

This document presents that estimate for Fiscal Years 1997/1998. The following pages describe the resources needed to sustain current successful efforts. In addition, we identify five areas of unprecedented cancer research opportunity which, if exploited, will greatly increase our capacity to reduce suffering due to cancer. This document describes these opportunities, the NCI's goals and plan for meeting the goals in each area, the additional investment required to turn this promise into progress, and the greater cost to the Nation if we do not act.

This budget represents an investment in research, but more importantly an investment to improve the Nation's health. Most importantly, it is an investment in hope—the hope that springs from the discovery of the tools and knowledge that we must have to reduce the awful burden of cancer.

In addition, this document discusses significant expansion of the Nation's cancer research investment to capitalize on the recent advances—in understanding the genetic basis of cancer, in the development of early detection techniques, and in the accurate description of the behavior of each cancer in each affected individual—and to determine the implications of these advances for prevention, detection, diagnosis and treatment.

In summary, the budget request for the NCI is as follows:

**FY 1997/98 BYPASS BUDGET REQUEST
(ESTIMATE—CONTINUING RESOLUTION)**

FY 96 \$2,251,084

FY 97 \$2,281,000 (Estimate)

FY 98 \$2,433,000 (Maintenance *)

FY 98 \$2,702,500
(Total: Maintenance plus
\$269,500 Investment)

*Includes inflation and program growth

All figures are dollars in thousands

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The National Cancer Institute (NCI)

An Institution Dedicated to Discovery

The NCI is the core of this Nation's response to cancer. Science is the way we understand the natural world, and the NCI is an institution of science dedicated to discovery about all aspects of cancer. Its work is based on the premise that we must know what causes cancer in order to prevent it and we must know the nature of cancer in order to accurately detect, diagnose, and treat it.

Research is the process by which questions about cancer are asked and answered. These key questions include:

- **Nature of Cancer:** What is cancer and how does it develop?
- **Cancer Risk:** Who is at risk for which cancers and why?
- **Prevention:** How can cancer be prevented?
- **Detection:** How do we screen for, detect, and diagnose cancer?
- **Treatment:** How do we best treat cancer?
- **Rehabilitation:** How do we improve quality of life for cancer patients and survivors?

While we have made progress in answering these questions, the burden of cancer continues.

Progress Against Cancer

We measure progress against cancer in terms of:

- The growth of knowledge about cancer and
- The reduction of the cancer burden.

The Growth in Knowledge

Twenty-five years ago three theories of cancer (one based on viral causes, one based on heredity, and a third based on chemical causes) dominated cancer research, but there was little direct evidence for any of these theories for the vast majority of human cancer.

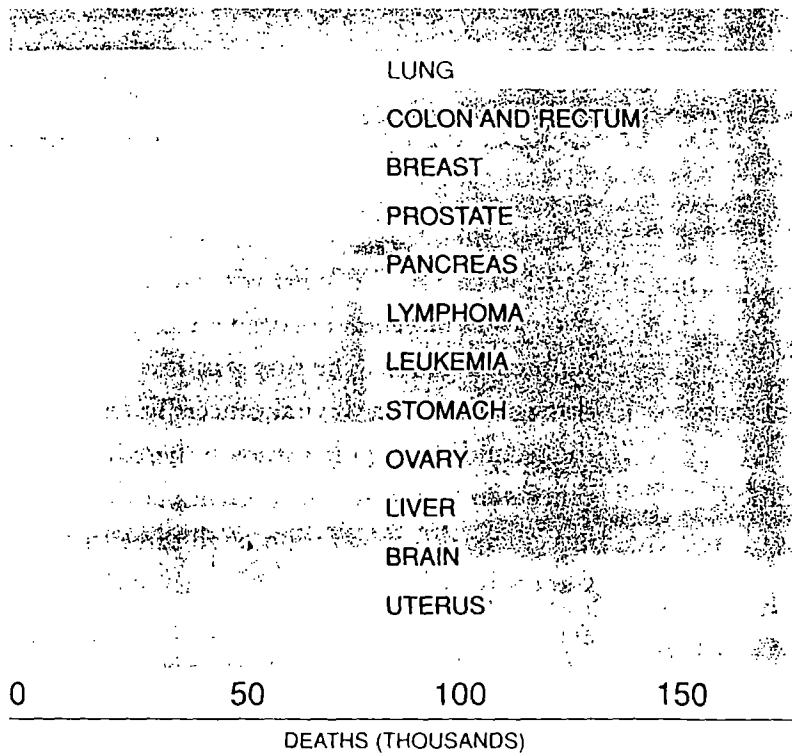
WHAT IS CANCER?

Today we know that cancer is a group of diseases that results from a series of changes in genes that control cell growth and behavior. These genetic changes transform a healthy cell, or one that has inherited a predisposition to these changes, into a cancer cell. One of the critical questions in cancer research is how and why these genetic errors occur, and just as important, why the errors are not corrected by the cell's normally efficient surveillance mechanisms. The relationship of these genetic changes to the environment, and to behaviors such as diet and smoking, is especially important. Smoking is the cause of more than 30 percent of cancer deaths, and diet may be implicated in an even greater number of cancers. The origins of this group of diseases lie in the interplay between the vulnerability of our genetic material, DNA, and the challenges and stresses that environment places on the cells in which DNA is housed.

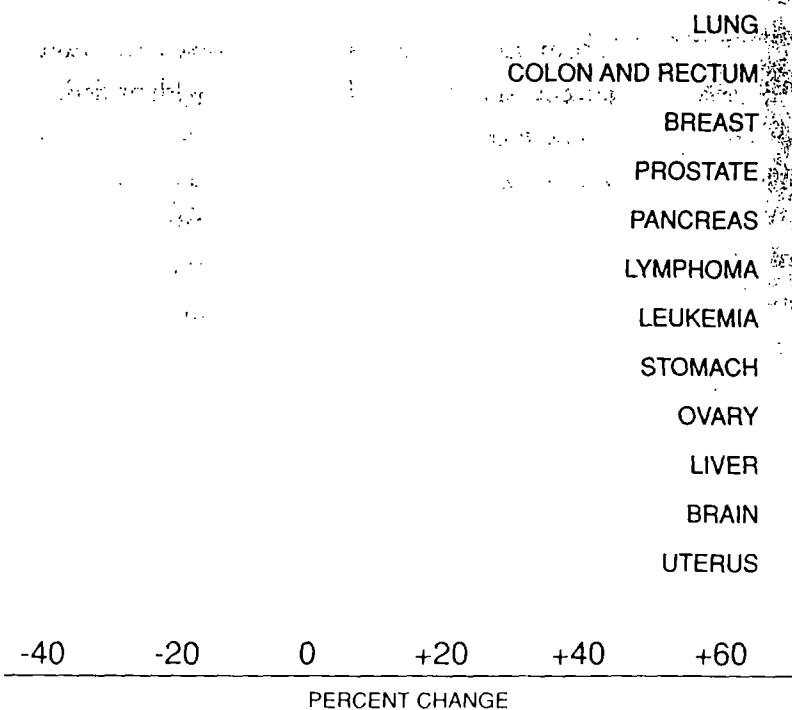
All of that has changed with the discovery of two classes of genes, oncogenes and tumor suppressor genes. The first was discovered through the study of viral cancers in animals, the second through the study of hereditary cancers in humans. The present view of cancer has emerged from a fusion of all three theories. Cancer is a disease of altered genes and altered gene function. These alterations can be inherited or acquired as the result of chemical or physical damage or the effects of viruses.

These new developments in our understanding of cancer are extending to all forms of human cancer. At first, the genetic basis of cancer was observed in certain rare cancers, but now these insights are extending to the most common cancers. Genes whose dysfunction leads to cancer are being rapidly identified. These genes ultimately determine the behavior and the relentless growth of cancer cells. Some of these genes, the oncogenes, can be activated inappropriately, similar to the uncontrolled accelerator of an automobile. Conversely, the tumor suppressor genes, or anti-oncogenes, can lose their function, like defective automobile brakes. Our knowledge about these genes is still incomplete, and many cancer genes remain to be found. Ideas abound on ways to use the new information for cancer prevention, diagnosis, prognosis, detection, and treatment. In short, the whole field of cancer research has been revolutionized and energized by this recent and continuing genetic revolution.

ESTIMATED CANCER DEATHS, 1996



CHANGE IN CANCER DEATH RATE (1973-92)



Reducing the Burden—the NCI's Ultimate Goal

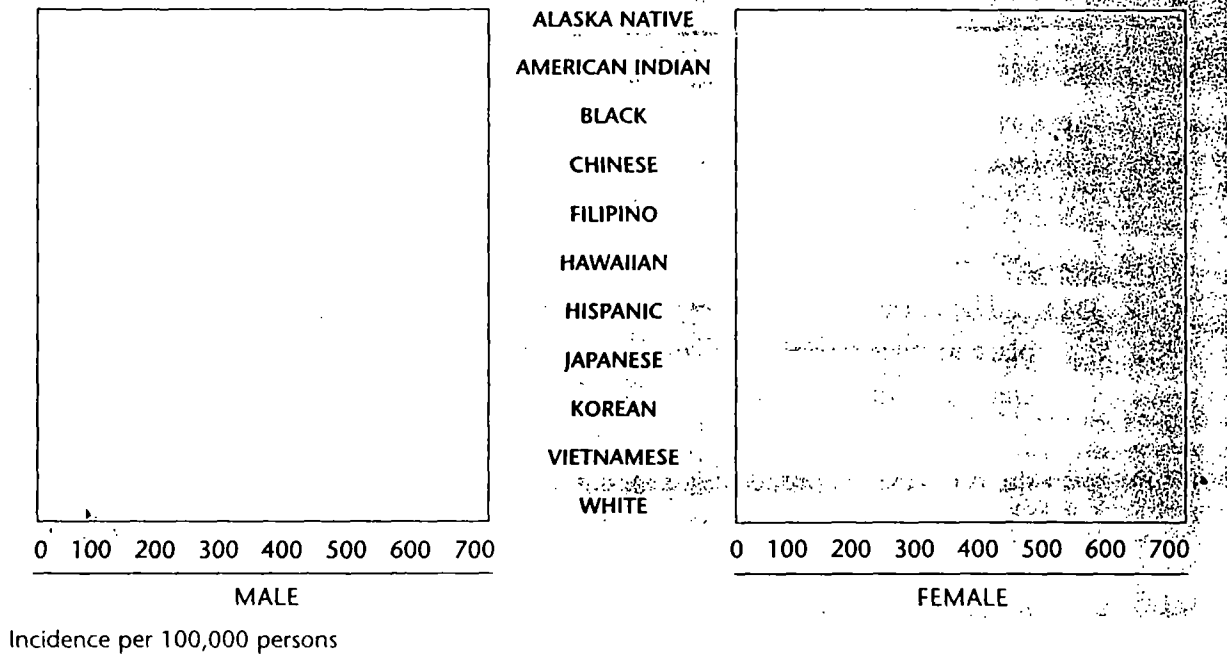
Reducing the burden of cancer can be measured in terms of fewer deaths, fewer new cases, increased length of survival, and increased quality of life of cancer survivors.

For several cancers, decreasing death rates reflect cumulative research successes during the past 25 years: death rates from children's cancers have declined by more than 50 percent, and with advances in chemotherapy, hormonal treatments, and in the access to and use of screening mammography, breast cancer mortality has finally begun to decline—down five percent since 1989. Deaths from colon and rectal cancers have dropped steadily, declining 10 percent in the past 25 years, and mortality rates have also decreased for Hodgkin's disease and testicular cancer, both due to dramatic advances in therapy.

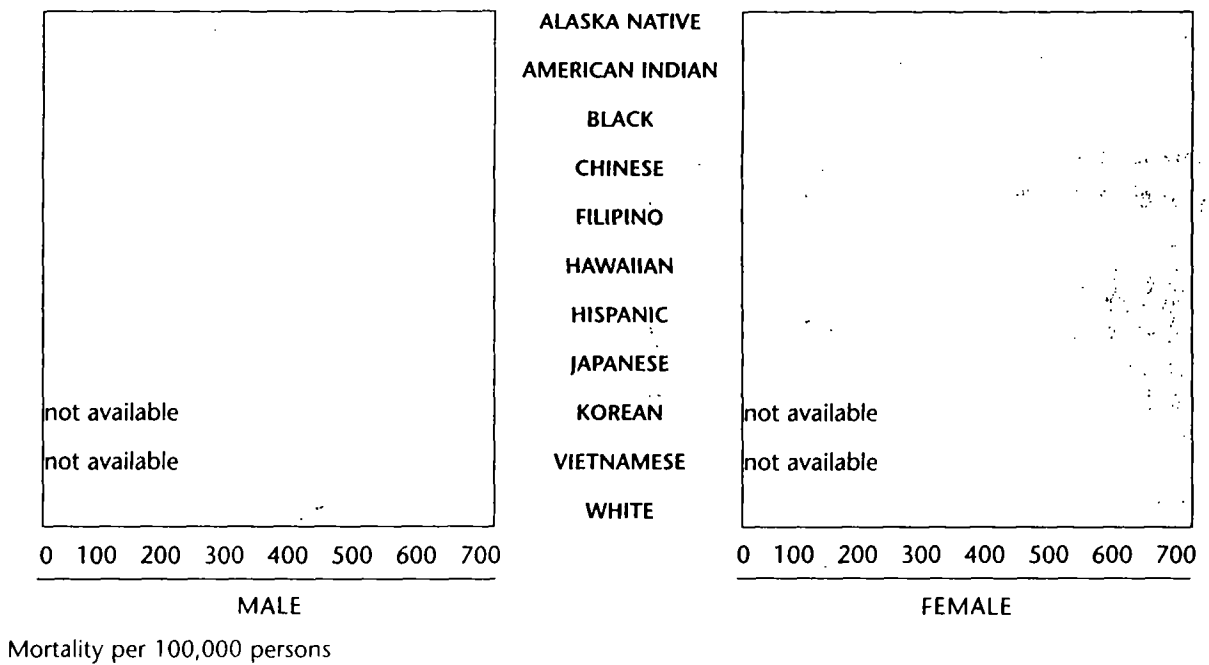
After a formidable battle to reduce the prevalence of cigarette smoking, lung cancer rates for men have declined. As smoking rates among women have increased, however, their lung cancer mortality rates have risen alarmingly. For other cancers, including non-Hodgkin's lymphomas, melanoma, brain, kidney, and prostate cancers, mortality rates have not fallen or are increasing. Particularly disturbing are the higher incidence and mortality rates for several ethnic and racial minority populations.

In addition to improvements in mortality rates for many malignancies, we have achieved important improvements in the quality of life for cancer survivors through less disfiguring and less damaging surgical procedures, better pain control, and more effective medication for the side effects of cancer therapy.

CANCER INCIDENCE, 1988-1992, BY RACIAL AND ETHNIC GROUPS



CANCER MORTALITY, 1988-1992, BY RACIAL AND ETHNIC GROUPS



Yet, even taking into account these advances, overall cancer incidence continues to increase, emphasizing the formidable task ahead. The goal of a reduced cancer burden

can only be achieved by the successful translation of discoveries to the benefit of all people who are at risk for and who have cancer.

DRAFT

Budget Summary

National Cancer Institute 1997/98 Bypass Budget Request

PRINCIPAL BUDGET COMPONENTS

(dollars in thousands)

	1995 ACTUALS	1996 ESTIMATE	1997 ESTIMATE	1998 MAINTENANCE
Research Project Grants (RPGs):				
Ongoing.....	\$703,149	\$730,020	\$797,014	\$876,714
New (New and Renewal)	261,677	295,007	252,085	267,140
Small Business Innovation Research ...	32,485	34,479	42,479	44,603
Subtotal.....	997,311	1,059,506	1,091,578	1,188,457
Intramural Research*	391,084	405,203	398,286	407,200
Cancer Centers	157,164	167,507	167,530	175,898
Clinical Trials Infrastructure:				
Clinical Cooperative Groups	75,192	89,226	89,226	98,687
CCOPs	39,329	38,696	41,212	42,654
Subtotal.....	114,521	127,922	130,438	141,341
Training and Education	67,411	72,126	71,645	81,215
Research Support Contracts*	252,025	278,791	281,007	291,447
Cancer Control:				
Grants**	62,167	78,854	81,220	85,281
Contracts***	99,481	115,947	114,594	120,324
Research Support	30,627	30,199	31,686	33,270
Subtotal.....	192,275	225,000	227,500	238,875
Research Management & Support	108,059	100,831	100,831	105,873
Other****	12,700	8,999	7,999	8,299
Total NCI	\$2,130,902	\$2,251,084	\$2,281,000	\$2,433,000

* Approximately \$20 million of additional Intramural Support is included within Research Support Contracts

** Included within Grant Categories

*** Included within Research Support Contracts Category

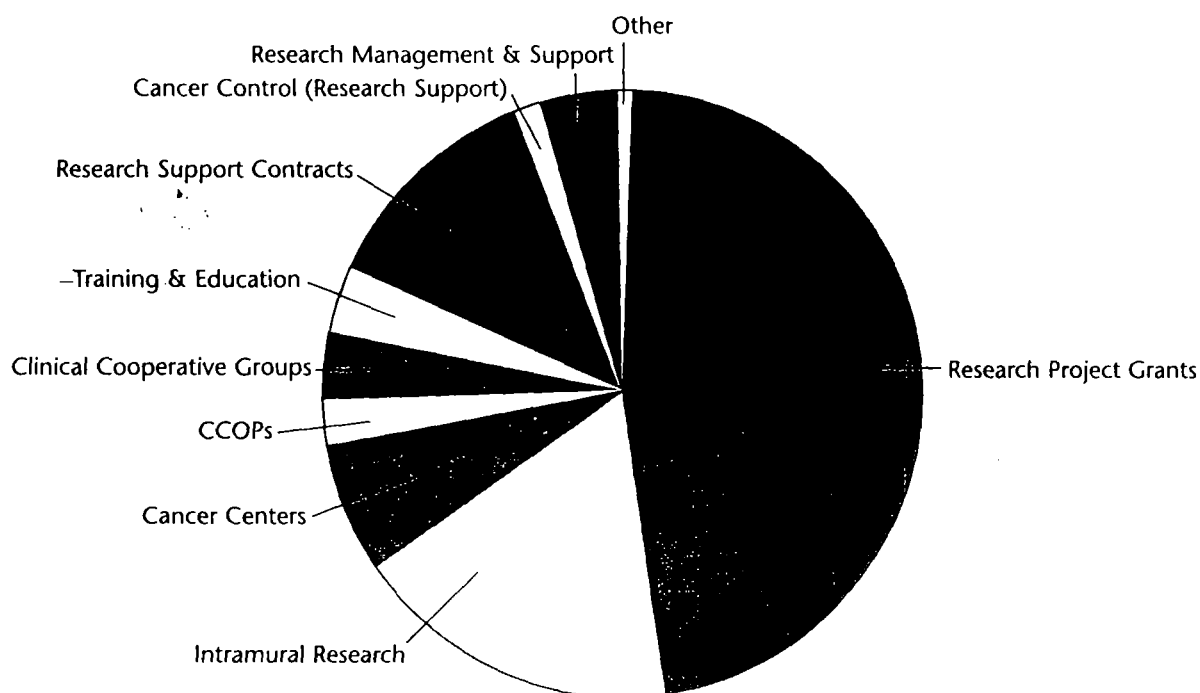
**** Includes Construction, Continuing Education, Scientific Evaluation and Scientific Conferences

Notes: 1. AIDS research dollars are distributed throughout Principal Budget Components

2. 1996, 1997 and 1998 Estimates reflect the impact of a pending FY 1996 reprogramming

FY 1997/98 Bypass Budget Request

FY 1997 Estimate: \$2,281,000



Dollars in Thousands

FY 1997 Estimate:

Research Project Grants (RPGs).....	\$1,091,578
Intramural Research	398,286
Cancer Centers	167,530
CCOPs	41,212
Clinical Cooperative Groups.....	89,226
Training and Education.....	71,645
Research Support Contracts	281,007
Cancer Control (Research Support)	31,686
Research Management & Support.....	100,831
Other	7,999
TOTAL.....	\$2,281,000

Extraordinary Opportunities for New Investments

What makes a new research opportunity worthy of our investment? The NCI continues to support superlative studies in all areas of basic, clinical, and population-based cancer research. These studies continue to be highlighted by spectacular advances in both our knowledge of how cancer occurs and in better clinical care. However, in preparing this budget it became clear that there were several areas where our efforts were not sufficient to exploit a particular research development. Several of these areas provide the opportunity to invest in the research future. To document the unique nature of these extraordinary opportunities for new investments, we have presented them as a special addition to this budget document. Included below are the plans for these areas, including the goals of each of these projects and the milestones to judge their success.

These areas for investment were discovered through a simple process. For the last six months we have been gathering with scientists, educators, and community leaders to discuss the state of our cancer research enterprise. At each setting we have been probing the collective wisdom of the group with many questions. One difficult question was, "Where are we failing?" Hearteningly, we have found that our most serious failures are primarily ones of omission, that is, where we are failing to pursue promising leads. Some of these we can correct by simple re-directions of our efforts, and even now most of these are on their way to being remedied.

Some of the omissions were of a different

flavor. Perhaps there was some new technical advance that we weren't exploring fully or maybe our knowledge had reached a stage where we could plan a new attack and, by doing so, catapult our knowledge to a new level. Over the six months of these discussions, 60 different proposals for new opportunities came forth. As the subjects of these 60 were explored, criticized, and refined, we realized that they were often different views of the same issues. Sixty quickly coalesced to five. The five programs that deserve immediate investment are:

- Cancer Genetics
- Preclinical Models of Cancer
- Detection Technologies
- Developmental Diagnostics
- Investigator-Initiated Research

These are the five areas where we believe new investments will pay the largest dividends. They are, in many ways, new windows of discovery that have been opened through past successes.

The Criteria for an *Extraordinary* Opportunity for Investment

In proposing these initiatives, we found that to be considered for an extraordinary opportunity for investment, the initiatives had to meet several criteria. The initiatives had to respond to an opportunity opened by a recent change or development. The initiatives we propose are responses to recent advances in our knowledge such as the rapid identification of new cancer genes, to recent technological breakthroughs such as the ability to develop

INVESTMENT OPPORTUNITIES: PROPOSED FUNDING

	FY 98	FY 99	FY 00
Cancer Genetics	\$31.5	\$49	\$68.5
Clinical Models of Cancer	15	32.5	40
Detection Technologies			
Signatures of Cancer Cells	30	38.5	46
Diagnostic Imaging	39	48	58
Developmental Diagnostics	79	91	102
Investigator-Initiated Research	75	138	204
TOTAL	\$269.5	\$397	\$518.5

Dollars in Millions

preclinical models of cancer, or to looming social responsibilities such as the issues raised by genetic testing. The initiatives had to provide approaches that go beyond the size and scope of our current portfolio of research activities but still be ones that could be capitalized with specific, defined investments. The five areas we have identified can be enacted with a total of 269.5 million dollars of additional, new funds in FY 1998. The derivation of this budget is described in each section below. The opportunities had to be articulated in goals with achievable milestones, which appear in each section. Finally, we found it essential to be able to describe both the benefit of investing in these new opportunities as well as the consequences of waiting or not investing. Again, this information is included below in the discussions of each opportunity.

Clearly there is a vast number of opportunities for investment in cancer research. We have touched on but a few of these in outlining what is supported by the Estimated Budget for FY 1997 and the Maintenance Budget for FY 1998. But we feel these five opportunities warrant substantial new invest-

ments—investments that will expand the budget beyond its current level. We must not lose sight, however, that investment is always underway. Each year a substantial portion of our research portfolio produces discoveries that new research builds on. Research today is supplanted by new projects tomorrow. For example, our gains in improving current therapies and establishing the efficacy of new therapies have been built on two decades of investments in the Clinical Trials Cooperative Groups, the CCOP, Cancer Centers, and individual and program project grants. We will continue to monitor discoveries across the cancer program and evaluate with our advisors where new investments will expand the research program in new dimensions that we believe hold enormous potential for success when built on the current discovery base.

Our goal is to assure that the Nation's cancer research resources are used as effectively as possible.

For the five areas that are ready for investment, with additional resources, the NCI will be able to:

- In cancer genetics—expand and integrate basic, clinical and epidemiologic research, facilities and training in cancer genetics to identify and characterize genes responsible for inherited predisposition to cancer; develop diagnostic tests for alterations in these genes; provide training in genetic counseling and in cancer genetics for health professionals; and develop the informatics for collecting, storing, analyzing and integrating the resulting molecular, epidemiologic and clinical data. *Goals: Identify within 5 years every major human gene predisposing to cancer; transform medical practice with this knowledge; and address the psychosocial, ethical and legal issues associated with cancer genetics.*

- In preclinical models of cancer—develop new preclinical models of cancer to study

mutations likely to drive human cancers, provide a natural setting for studying all stages of tumor development, and allow testing of cancer prevention and detection strategies, as well as new treatment regimens. *Goals: Create animal models of human cancers and build the experimental foundation to use these models effectively, and to develop the infrastructure and procedures to make these models available to all researchers.*

■ In detection technologies—improve early detection methodology through identification of the unique secreted proteins and mutant genes in body fluids after exposure to tumor cells as well as improve diagnostic imaging technology to become more sensitive and specific in order to detect the fewest number of tumor cells possible. Early detection of tumor products in a blood sample could signal the presence of small numbers of tumor cells, providing opportunities to detect tumors at their earliest stages. *Goals: Develop new methodologies that will allow the detection of much smaller numbers of tumor cells than ever before; discover and develop techniques that will further increase the precision, accuracy, and scope of imaging diagnosis; and integrate imaging further into the practice of clinical oncology.*

■ In developmental diagnostics—improve and expand the diagnosis of cancer by applying molecular characterization of cancer cells to fundamentally change the care of cancer patients. The understanding of tumor properties will detail key differences between a normal and cancer cell, providing a molecular profile. This profile can then be used to develop and choose effective therapies and to plan patient care. *Goals: Develop diagnostic tests that will allow treatment choice to be based on the fundamental properties of a tumor cell.*

■ In investigator-initiated research—expand investigator-initiated research by funding a higher percentage of grant applications.

Goals: Expand the number of investigator-initiated research pool grants by over 30 percent, to capture the opportunities of the new ideas as rapidly as possible.

OPPORTUNITY 1

Cancer Genetics

Years of intensive research have enhanced our understanding of how tumors develop. First and foremost, we have learned that cancer is a genetic disease. Mutations in our own genes drive the development of cancer. These mutations alter the normal processes that help a cell regulate its fate. When these processes are disrupted, control is lost and tumor development is promoted. Second, we now understand that a cancer will arise only after several mutations occur in the same cell. One mutation is never sufficient, and in some adult cancers ten or more mutations may be needed to generate the full set of changes that make tumors aggressive. Third, we have learned that the number of different genes that can be mutated and contribute to all types of cancer is large (although for a specific cancer, the number may be no more than 10 altered genes). Certainly the number of genes involved in cancer overall will be in the hundreds; our current knowledge suggests that the number will not reach 1,000. These numbers are large, daunting perhaps, but not impossible to handle. These three major discoveries explain the fundamental genetic basis of tumor development. Cancer is a disease caused by mutations in key target genes that give selective advantage to the growth of the tumor cell. The accumulated mutations allow the cells to grow out of control. They divide, obstruct, invade, and destroy normal tissue architecture. Through

CLONED FAMILIAL CANCER GENES

GENETIC CONDITION	MAIN CANCERS	GENE	LOCATION	YEAR
Hereditary retinoblastoma	Retinoblastoma Sarcomas	RB1	13q14	1986
Hereditary Wilms tumor	Wilms tumor	WT1	11p13	1990
Li-Fraumeni syndrome	Breast Cancer Sarcomas Brain tumor	TP53	17p13	1990
Neurofibromatosis 1	Sarcomas Brain tumor	NF1	17q11	1990
Familial adenomatous polyposis	Colon Cancer	APC	5q21	1991
Neurofibromatosis 2	Acoustic neuroma Brain tumor	NF2	22q12	1993
von Hippel-Lindau syndrome	Renal Cancer Pheochromocytoma Brain tumor	VHL	3p25	1993
Multiple endocrine neoplasia 2	Pheochromocytoma Medullary thyroid cancer	RET	10q11	1993
Tuberous sclerosis 2	Renal Cancer Brain tumor	TSC2	16p13	1993
Hereditary non-polyposis Colon Cancer 1	Colon Cancer Endometrial Cancer Stomach Cancer	hMSH2	2p16	1993
Hereditary non-polyposis Colon Cancer 2	Colon Cancer Endometrial Cancer Stomach Cancer	hMSH1	3p21	1994
Hereditary non-polyposis Colon Cancer 3	Colon Cancer Endometrial Cancer Stomach Cancer	hPMS1	2q32	1994
Hereditary non-polyposis Colon Cancer 4	Colon Cancer Endometrial Cancer Stomach Cancer	hPMS2	7p22	1994
Hereditary Melanoma 1	Melanoma	CDKN2	9p21	1994
Hereditary Breast Cancer 1	Breast Cancer Ovarian Cancer	BRCA1	17q21	1994
Ataxia telangiectasia	Breast Cancer Lymphoma	ATM	11q22-23	1995
Hereditary Breast Cancer 2	Breast Cancer	BRCA2	13q12-13	1995
Hereditary Melanoma 2	Melanoma	CDK4	12q13	1996

two different sets of cancer genes, one group for inherited predisposition and one for sporadic tumor development. The mutations that drive inherited predisposition are at least a subset of the ones that spur all human tumor development.

These revelations in cancer genetics have convinced us that this area is an under-explored gold mine. They also have provided an important lesson: Use the rare predisposition genes to learn more about common cancers. This lesson is a guidepost for future research, and the cancer genetics initiative proposes a plan to exploit this lesson.

The opportunities afforded by advances in cancer genetics also raise enormous challenges. What are the psychological, social, family, and medical consequences of being able to determine inherited susceptibility to cancer? The cancer genetics investment initiative must also address these issues to ensure that individuals are helped, not harmed, by personal genetic knowledge.

The Plan

To capitalize on these unprecedented opportunities and to address the diverse challenges in cancer genetics, support is needed for new activities in five areas.

- We need to support the identification of high-risk families and the infrastructure required to identify and characterize cancer predisposition genes.
- We need to support the development of accessible and reliable diagnostic tests for alterations in these genes.
- We need to provide greatly increased resources to support clinical research and trials to answer the key questions about inherited mutations in these genes, including:
 - What is the risk over time of developing cancer in different individuals who inherit

different mutated forms of a particular cancer gene?

- Are there prevention strategies that might reduce the risk of cancer in these individuals?
- What are the efficacies of surveillance and detection strategies?
- What treatments are best for those individuals who develop cancer?
- What are the ethical and psychosocial issues that will affect healthy individuals and their families in whom an inherited predisposition to cancer may be detected? How can they be resolved?
- How can people be helped to make informed decisions about testing for genetic susceptibility?

■ The enormous impact of genetics in oncology requires support for education and training. Educational materials aimed at the public, physicians and other health providers and payers are needed. A new medical work force with expertise in genetics and counseling is required.

■ Successfully dealing with these challenges will involve generating and analyzing enormous amounts of data about dozens of genes and hundreds of alterations in each gene plus correlating each of these alterations with clinical outcomes. Therefore, the fifth area of the cancer genetics initiative is to develop an informatics system to collect, store, analyze, and integrate molecular data with epidemiologic and clinical data. Only a useable informatics infrastructure will allow progress to affect all aspects of cancer research. For example, as new families that suffer a predisposition to cancer are identified, the properties of their disease need to be passed to the researchers who will map the gene. Basic researchers' discoveries about how a tumor develops must be passed on to those who treat and counsel