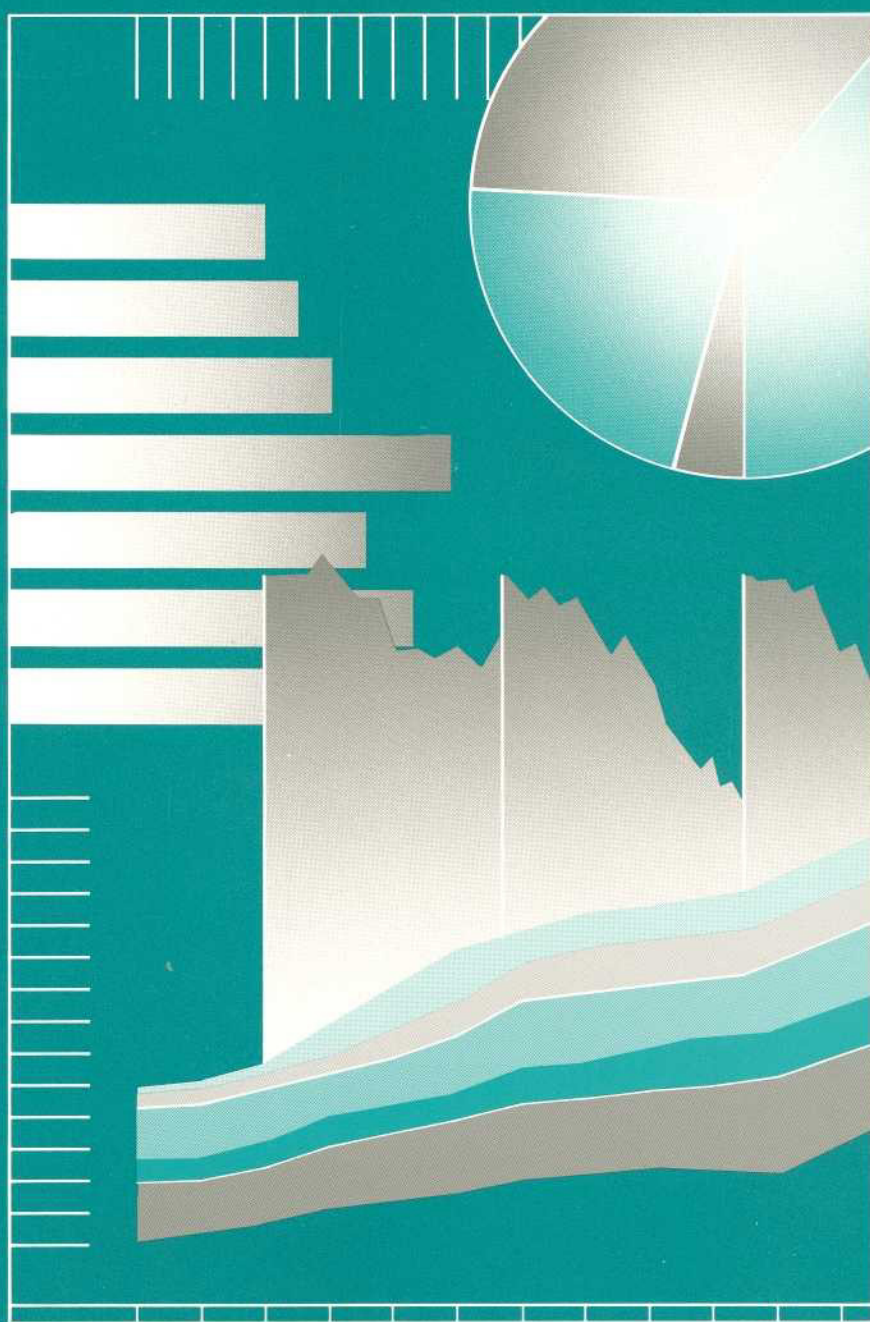


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The information set forth in this publication is compiled and amended annually by the financial management staff of the National Cancer Institute and is intended primarily for use by members of the Institute, principal advisory groups to the Institute and others involved in the administration and management of the National Cancer Program. Questions regarding any of the information contained herein may be directed to the Financial Management Branch, National Cancer Institute, 9000 Rockville Pike, Bethesda, Maryland, 20892.

TABLE OF CONTENTS

| | Page |
|--|--|
| Prologue | Significant Initiatives 1 |
| | Public Information Dissemination 16 |
| Organization | Directory of Personnel 17 |
| | National Cancer Institute Leadership: |
| | Director's Biography 20 |
| | Former Directors of the NCI 21 |
| | National Cancer Advisory Board 22 |
| | Division Boards of Scientific Counselors 23 |
| | President's Cancer Panel 24 |
| | Executive Committee Members 24 |
| | Organization Charts: |
| | National Cancer Institute 25 |
| | Office of the Director 26 |
| | Division of Cancer Biology, Diagnosis, and Centers 27 |
| | Division of Cancer Treatment 28 |
| | Division of Cancer Etiology 29 |
| | Division of Cancer Prevention and Control 30 |
| | Division of Extramural Activities 31 |
| | Information Flow for Program Implementation 32 |
| | Intramural Review Process 33 |
| | Research Positions at the National Cancer Institute 34 |
| | Cancer Statistics |
| Relationship of Cancer to the Leading Causes of Death in the U.S. 47 | |
| Estimated New Cancer Cases and Deaths 48 | |
| The Cost of Cancer 49 | |
| Average Years of Life Lost Per Person Due to Cancer Deaths 50 | |
| Five-Year Relative Survival Rates by Cancer Site 51 | |
| Cancer Mortality Rates: | |
| Changes by Year: | |
| Ages Under 65 52 | |
| Ages Over 65 53 | |
| United States 54 | |
| Cancer Incidence Rates 55 | |
| The Prevalence of Cancer 56 | |
| Budget Data | NCI Budget 57 |
| | Program Structure 58 |
| | Research Programs 59 |
| | Extramural Funds 60 |
| | Total Dollars by Mechanism 61 |
| | Division Obligations by Mechanism 62 |
| | Reimbursement to NIH Management Fund 63 |
| | Special Sources of Funds 64 |

| | <u>Page</u> |
|---|-------------|
| AIDS | |
| Key Discoveries | 65 |
| AIDS Funding: | |
| By Activity | 70 |
| Funding History | 71 |
| Extramural Programs | |
| Grant and Contract Awards by State | 73 |
| Foreign Research Grants and Contracts | 74 |
| Institutions Receiving More than \$5,000,000 in NCI Support | 75 |
| Cancer Centers: | |
| Funding History | 76 |
| By State (P30 Core Grants) | 77 |
| Specialized Programs of Research Excellence (SPORE) | 78 |
| Research Project Grants: | |
| Requested, Awarded | 79 |
| Success Rate | 80 |
| Adjustments From Recommended Levels | 81 |
| Number of Awards | 82 |
| History by Activity | 83 |
| National Research Service Awards | 84 |
| Construction/Renovation Funding | 85 |
| Selected Minority-Focused Activities | 86 |
| Historical Trends | |
| Appropriations of the NCI | 91 |
| Bypass Budget Requests | 92 |
| Comparison of Dollars, Positions and Space | 93 |
| Personnel Resources | 94 |
| Obligations and Outlays | 95 |
| Constant Dollar Trends | 96 |

Significant Initiatives in 1994

Division of Cancer Biology, Diagnosis, and Centers

Characterization of Genetic Alterations Associated with Familial Colorectal Cancer

Characterization of the genetic alterations underlying hereditary non-polyposis colon cancer, HNPCC, has identified an important new pathway of cancer pathology. Mutations in two genes, hMSH2 and hMLH1, are associated with a high percentage of HNPCC cases. The genes encode enzymes involved in DNA repair, and mutations in these genes result in generalized genomic instability. This instability is characterized by amplifications and deletions of small repeated sequences scattered throughout the genome, resulting in disruption of normal functions. These alterations can serve as a marker for identifying members of HNPCC families with increased risk of disease. The role of these genes in sporadic cases of colon cancer is being evaluated, and recent evidence has suggested that genomic instability may play a significant role in tumors of other organs as well. Further study is needed to confirm that genomic instability is an important mechanism in cancer pathology.

Cloning of Familial Breast Cancer Gene: BRCA1

The BRCA1 gene, located on chromosome 17, is estimated to underlie about half of early-onset familial breast cancer. Investigators recently cloned the gene which will allow them to identify the range of alterations associated with familial breast cancer. This information can then be used to develop diagnostic tests that will identify women in these families who are at increased risk. These investigators have also identified a region on chromosome 13 that contains a second familial breast cancer gene, BRCA2, and are attempting to identify and clone the relevant gene. Although a small, preliminary study suggested that BRCA1 mutations are uncommon in sporadic breast cancers, further study will be necessary to determine whether the gene plays a role in sporadic disease.

Enhanced Understanding of the Control of Programmed Cell Death (Apoptosis)

Understanding of the control of programmed cell death (apoptosis) by the Bcl-2 proto-oncogene product has been enhanced by the recent discovery of a family of Bcl-2-related proteins that interact with each other and play a role in both positive and negative regulation of apoptosis. The bcl-2 gene, discovered at the t(14;18) chromosomal translocation breakpoint found in most follicular B-cell lymphomas, is the first proto-oncogene that has been shown to cause tumors by blocking apoptosis. It was shown to prevent apoptotic cell death in cultured cells deprived of growth factors. However, bcl-2 is not able to block apoptosis induced by cytokine deprivation or receptor-mediated signaling in all *in vitro* cell culture systems. *In vivo*, bcl-2 prevents many, but not all, forms of apoptotic cell death that occur during lymphoid development. These results suggest the existence of either multiple independent intracellular mechanisms of apoptosis or additional

pathways which involve proteins that differentially regulate bcl-2 function. A search for additional members of the bcl-2 gene family and other apoptotic molecules will be the focus of further research effort in this field. Understanding how the various members of the Bcl-2 family interact with each other is vital in the elucidation of the basic mechanism of apoptosis.

Discovery of a Second Costimulatory Molecule for T Lymphocytes

Discovery of a second costimulatory molecule for T lymphocytes provides a new tool for enhancing the recognition of tumors by the immune system. T-cell activation is the critical step in the development of an effective immune response to a tumor. T-cell responses are normally antigen-specific because the most important activation signal comes from the interaction between the T-cell antigen receptor and an antigenic protein fragment displayed on the surface of an antigen-presenting cell (APC). However, full T-cell activation requires a second, or costimulatory, signal that is not antigen-specific. It is clear from many studies that the presence or absence of costimulatory signals can determine whether an immune response will occur and whether it will be effective. The major costimulatory signal receptor on T cells is known to be a molecule called CD28. Until recently, it was thought that the only ligand for CD28 was a molecule called B7, which is present on many APCs. Several groups have now shown that B7 (now renamed B7-1) is not the only ligand for CD28, and that a newly discovered molecule, B7-2, may be the more important co-stimulator of T cells under some conditions. Unlike B7-1, B7-2 mRNA is constitutively expressed in un-stimulated B cells. As such, it may provide the critical early costimulatory signal determining whether a T cell is stimulated or becomes paralyzed (anergic). The discovery of a second costimulatory molecule on APCs is prompting a reexamination of results obtained over the past few years on the failure of tumor cells to provide adequate co-stimulation to potential antitumor T cells.

Helper T Cells in Resistance to AIDS and Cancer

NCI scientists have found that the balance between certain subsets of helper T cells, in particular Th1 and Th2, could play a role in determining the type and effectiveness of the specific immune response generated against an infectious agent or a tumor. Stimulation of Th1 cells leads to the production of distinct set of cytokines and the promotion of cellular immunity, whereas stimulation of Th2 cells leads to the production of a different set of cytokines and the production of antibodies. Recent studies have demonstrated that cellular immunity, but not humoral immunity (antibody production), confers protection against the establishment of HIV infection and delays progression of infection to AIDS. HIV-exposed individuals who remain antibody-negative and free of clinical HIV disease generate brisk HIV-targeted Th1-type cytokine responses. Conversely, longitudinal studies of HIV-infected individuals demonstrate a shift in the Th1-Th2 balance toward a Th2-type cytokine profile. This switch correlates with a progressive loss of immune function associated with progression to AIDS. It has recently been shown that similar alterations in the Th1-Th2 balance occur in patients with certain types of cancer.

Division of Cancer Treatment

The Quality of Clinical Research

During the past year the quality assurance process of clinical research sponsored and supported by the National Cancer Institute have been subjected to intense scrutiny. Stimulated by the discovery of scientific fraud and misconduct a more

structured process was developed to report such events and a more comprehensive oversight process was initiated as a prevention measure to include the creation of a new branch within a Cancer Therapy Evaluation Program, the Clinical Trials Monitoring Branch

A comprehensive examination is under way on how to monitor clinical trials and track and maintain quality assurance. Committees of Extramural Consultants, the Cooperative Clinical Trials Groups and Intramural NCI staff are meeting to develop new, more effective and efficient mechanisms for assuring that the conclusions of clinical trials are accurate.

Drug Discovery

For several years, initial *in vitro* screening of new agents for anticancer and anti-HIV activity has been carried out utilizing standardized procedures, at an annual input level of about 10,000 synthetic compounds and an equal number of natural product extracts. The cancer screen has utilized a panel of 60 human tumor cell lines which initially represented seven tumor categories, lung, colon, renal, melanoma, CNS, ovarian, and leukemia. Although of great clinical importance, breast and prostate lines were not included initially because of difficulty in developing suitable cell lines. During the past year, both breast and prostate cell lines have been incorporated into the cancer screening panel. In addition, testing against a separate panel of prostate cell strains and testing against AIDS-related lymphoma cell lines has been implemented. It is of interest that a substantial portion of the agents demonstrating patterns of activity against the breast cancer lines appear to be tubulin-interactive agents, an observation that will be explored further.

A considerable effort, involving intramural, extramural, and collaborative investigators, has been devoted to the characterization of the 60 human tumor cell lines with regard to specific molecular targets, such as multi-drug resistance, p53, bcl-2, ras, etc. Utilizing the COMPARE computer analysis, it has been possible to develop patterns of cell line sensitivity representative of these targets so that new compounds can be detected with patterns peculiar to a target. Mechanisms are now being developed to implement this approach and carry out confirmatory testing in the target model. Materials found to affect a specific target can then be directed toward specific groups of patients, and combination therapies developed to take advantage of this information.

Vaccine Development

Researchers in NCI's Surgery Branch, Clinical Oncology Program have identified the antigen recognized by T-lymphocytes which mediate tumor rejection in man. This work was done by constructing a library from the DNA of a melanoma which responded dramatically to treatment with Tumor Infiltrating Lymphocytes (TIL) and interleukin-2. The genes from this library were then inserted, one at a time, into a MHC-identical melanoma cell line resistant to TIL therapy. This technique allowed the isolation, cloning and expression of MART-1 (Melanoma Antigen Recognized by T-cells). Important, co-incubation of naive peripheral lymphocytes with MART-1 converts them into high efficiency lytic cells specific for that tumor. MART-1 is currently under study for its potential to prevent and treat malignant melanoma.

Vaccine Studies

Animal studies have been performed demonstrating that mice can be protected against a tumor transformed by a mutant ras oncogene by immunization with the free mutant ras protein. The immunity elicited is specific for tumor cells expressing the same mutation as the protein used for immunization. Nearly 40 percent of human cancers contain a mutated ras oncogene, with the mutations clustering around changes in codons 12, 13, and 61. Purified mutant ras oncoproteins have been generated for administration to humans and are about to begin a clinical trial evaluating whether patients with tumors expressing a mutated ras protein may develop immunity after immunization with mutant ras protein.

Lymphoma Idiotype Antigen Vaccines

The idiotype of the surface immunoglobulin molecule expressed by a given B-cell malignancy can serve as a unique tumor-specific antigen (Id). A pilot study in humans has already demonstrated that this autologous protein can be formulated into an immunogenic therapeutic vaccine, and tumor regressions were observed. The goals for vaccine development at the NCI in larger-scale clinical trials based on preclinical studies are: 1) the development of vaccine formulations which are more effective in activating the cellular arm of the immune system, and 2) to increase vaccine potency.

The first phase II clinical trial is testing Id in combination with adjuvants designed to induce primarily T-cell responses (IL-2 and GM-CSF) in newly diagnosed patients with low-grade follicular lymphomas in first remission following ProMACE induction chemotherapy who have accessible lymph nodes as starting material for custom vaccine production. The clinical grade manufacturing process has been validated, and this trial is being conducted under an approved IND. Immunological, molecular, and clinical endpoints will be analyzed. At the close of 1994 13 patients were enrolled. Patient accrual is continuing in 1995.

DNA Repair Biology

Within the Clinical Pharmacology Branch extensive studies have been initiated on the human biology of nucleotide excision repair, in patients with ovarian cancer and patients with brain cancer.

Such studies have focused on the rate limiting step of nucleotide excision repair. This step is DNA damage recognition and excision, and appears to be mediated by genes of the ERCC and XP groups. Current data clearly demonstrates that in human ovarian cancer, genes involved in the first steps of nucleotide excision repair show the following patterns. ERCC1 (which affects DNA damage recognition and excision), ERCC3 (which affects linkage of DNA repair and DNA transcription), XPA (which "fine tunes" DNA damage recognition and localization), and ERCC6 (which affects gene specific repair), are all concurrently up-regulated in tumor tissues from ovarian cancer patients that are clinically resistant to platinum based therapy. These four genes are concurrently down-regulated in tumor tissues of patients that are clinically sensitive to platinum based therapy. Another feature seen in ovarian cancer patients is loss of concordant expression between ERCC1 and ERCC2. ERCC2 performs an important helicase function in nucleotide excision repair. This loss of concordant expression between ERCC1 and ERCC2 appears to be a feature of malignant ovarian cancer tissues, but is not seen in any of five different normal tissue settings that have been studied.

Similar patterns for the genes within the ERCC and XP groups have been observed in brain cancer patients. Also, in tumor tissues from patients with brain cancer, we have observed gene amplification of ERCC1 in brain cancer specimens, without concurrent amplification of ERCC2. This is particularly noteworthy since these two genes are approximately 200 kilobases apart on chromosome 19q.

Identification and Characterization of Plant-derived Proteins and Compounds with Potential Anti-HIV and Anti-Tumor Activities

Through collaborative studies several single-chain ribosome inactivating proteins (SRIP) have been identified from medicinal plants which inhibit HIV infection and replication. These plant proteins also exhibited growth-inhibitory effect on certain tumor cell lines.

Modulation of P-glycoprotein Mediated Drug Resistance by an Anti-tumor RNase *In vitro* and *In vivo*

NCI researchers have found that Onconase (a frog RNase), currently in clinical trials as an anti-cancer agent, enhanced vincristine and adriamycin cytotoxicity in cultured parental HT29^{PAR} and in drug resistant HT29^{MDR1} human colon carcinoma cells as well as in MCF-7^{Adr} human mammary cancer cells. The *in vitro* results were confirmed in nude mice given transplants of HT29^{MDR1} cells followed by treatment with a combination of vincristine and Onconase, thus establishing that Onconase can overcome drug resistance caused by the P-glycoprotein. This was the first study to establish Onconase as a chemosensitizer to VCR. Furthermore, Onconase was found to enhance the effectiveness of MRK-16, an antibody that reverses drug resistance. This observation was particularly interesting since combinations of MRK-16 with conventional chemosensitizers were not more effective than MRK-16 with single agents alone. Since Onconase does not cause myelosuppression, combination therapies are well tolerated in patients. Consequently, Onconase may present a viable new approach to treating the problem of drug resistance.

TGF β Abrogation of Chemotherapy-Induced Stem Cell Toxicity

Preclinical studies have shown for the first time that a negative regulator (TGF β) of hematopoiesis can be used to protect critical progenitor/stem cells from the destructive effects of chemotherapy. This observation has allowed the development of new strategies for the safe delivery of increased amounts of the cell-cycle active chemotherapeutic drug 5-fluorouracil in preclinical animal models. At the same time TGF β has been shown to also protect mice from some nonhematologic organ toxicity induced by doxorubicin. These findings suggest that TGF β may have protective effects for multiple organ systems against chemotherapy-induced toxicities.

Activation-induced Lymphoma Cell Growth Arrest

A number of signals that activate normal B cells result in the irreversible growth arrest (and sometimes apoptosis) of neoplastic B cells both *in vitro* and *in vivo*. For example, CD40, a receptor in the nerve growth factor/tumor necrosis factor receptor family, is universally expressed on normal and neoplastic B cells. Physiologically, it is involved in interactions of B cells with T cells. The CD40 ligand or an antibody of CD40 is capable of curing SCID mice bearing established human B cell lymphomas. We expect to bring this novel treatment strategy to clinical trials in the next year.

Allogeneic Marrow Donor Immunization Against Myeloma Idiotypic Antigen

Multiple myeloma remains a largely incurable disease with current therapy. The idiotype of the rearranged immunoglobulin gene product of a myeloma can serve as a unique tumor specific antigen for vaccine development. Immunization of a healthy donor, with subsequent adoptive transfer of anti-tumor immunity to the cancer patient, would represent a novel strategy. In collaborative trials with the University of Arkansas, we are testing the hypothesis that myeloma-specific immunity can be transferred from bone marrow transplant (BMT) donor to recipient at the time of BMT, thereby enhancing the specific antitumor effect of allogeneic marrow grafts.

This was accomplished in the first patient, whose HLA matched sibling donor was immunized with myeloma IgG, purified from the plasma of the BMT recipient, conjugated to a carrier protein, and emulsified in an adjuvant. Analysis of the BMT recipients peripheral blood mononuclear cells (PBMC) revealed a significant lymphoproliferative response to autologous idiotype 60 days after, but not prior to, BMT. An idiotype-specific T-cell line of donor origin has subsequently been established from recipient PBMC. Furthermore, the recipient experienced a clinical response to this therapy. We anticipate accrual of approximately 10-20 donor-recipient pairs per year who will be eligible to receive this therapy.

Progress Report for the Monoclonal Antibody/Recombinant Protein Production Facility (MARF)

The Biological Response Modifiers Program (BRMP) is establishing a biologics pharmaceutical production facility at the Frederick Cancer Research and Development Center (FCRDC), Frederick, Maryland. This facility will make biologic drugs available on a more predictable schedule and more economically than had been possible using outside vendors. These products will be made available to both intramural and extramural investigators on a priority basis determined by an expert review committee.

Division of Cancer Etiology

Inter-Agency Working Group on Breast and Gynecological Cancer

The NIH Revitalization Act of 1993 included language directing the NCI to coordinate research in breast and gynecological cancer across the PHS and other Federal agencies. The Inter-Agency Working Group, chaired by the Deputy Director of the Division of Cancer Etiology, has been established to fulfill this mandate. The Group's membership is broad-based, with representation from throughout the NIH as well as the PHS and other Government agencies. The Working Group has recently been designated by the Secretary, DHHS as the programmatic focal point for the coordination of activities and the dissemination of information under the National Breast Cancer Action Plan and will work in concert with the Department of Defense on the Army's Breast Cancer Research program.

The Long Island Breast Cancer Study Project

The Congressionally mandated Long Island Breast Cancer Study Project, conducted under the joint auspices of NCI and NIEHS, seeks to determine the relative contributions of diverse environmental factors to breast cancer risk in the New York counties of Nassau, Suffolk, and Schoharie and in Tolland county, Connecticut. This large epidemiologic study will examine a wide variety of environmental elements, including exposures to pesticides and other

organochlorine toxins, contaminated drinking water, indoor air pollution, aircraft and auto emissions, electromagnetic fields, hazardous waste and municipal waste. Dietary factors, radiation, estrogen exposures, and occupational exposures are also being assessed.

The Northeast/Mid-Atlantic Study

Also mandated by the Congress and jointly funded by NCI and NIEHS, the Northeast/Mid-Atlantic Study encompasses an area that covers the District of Columbia and nine states from Maryland to New England. The goal of this epidemiologic study is to define and quantitate the contributions of a number of environmental factors to breast cancer risk, with a particular emphasis on pesticide exposures.

The Agricultural Health Study

In collaboration with NIEHS and the EPA, a prospective cohort study of over 100,000 farmers and their families is underway to evaluate cancer and other disease risks associated with various agricultural exposures such as pesticides, herbicides, fertilizers, viruses, UV-light, chemical solvents and engine exhausts. An important component of the study involves the evaluation of cancer risks among women and children that may arise from indirect, nonoccupational exposures to agricultural chemicals such as ambient air drifts, handling contaminated clothing, and any residues found on rugs, children's toys, and in drinking water. Also under study is the identification and quantification of cancer risks associated with diet, various cooking practices, and chemicals resulting from the cooking process.

Migrant and Seasonal Farm Workers Feasibility Study

As a parallel project to the Agricultural Health Study, a feasibility study has been initiated to evaluate the potential for conducting a study of cancer risks from pesticides and other agricultural exposures that may affect migrant and seasonal farm workers and their families. Special efforts are being made to reach out to Hispanic and other minority farm workers so that their cancer experiences can be included for evaluation. The study will attempt to devise ways to surmount the practical difficulties associated with tracking these underserved populations, including the frequent migration of these groups between the U.S. and other countries and the barriers that prevent their use of the U.S. health care system.

A New Species of *Helicobacter*

A new species of *Helicobacter* (provisionally designated as *Helicobacter hepaticus* sp. nov.) that selectively and persistently colonizes the hepatic bile canaliculi of mice (and possibly the intrahepatic biliary system and large bowel) has recently been identified. The novel *Helicobacter* is a likely candidate for the etiology of the high incidence of a chronic, active hepatitis associated with hepatocellular tumors that was discovered in diseased mice at NCI's Frederick Cancer Research and Development Center in 1992. The *Helicobacter*-associated chronic active hepatitis represents a new model to study the mechanisms of carcinogenesis by this genus of bacteria, another species of which, *Helicobacter pylori*, is associated with gastric adenocarcinoma.

Cytochrome P450

Cytochrome P450s are involved in both steroidogenesis and steroid metabolism as well as in the metabolism and detoxification of drugs and other chemicals. One of the enzymes currently being studied is aromatase, the enzyme that converts androgens to estrogens. Because some cancers are estrogen dependent, this enzyme may prove to be a useful target for new chemotherapeutic compounds. In addition, 16 α -hydroxyestrone formation may be a biomarker for breast cancer. Ongoing studies are seeking to determine both estrogen synthesis and metabolism in human breast, ovary, cervical, and adipose tissues.

Heterocyclic Aromatic Arylamines

Ongoing studies on the metabolism and DNA adduction of heterocyclic amines (HAAs) have shown that these procarcinogens are produced in meats during the process of cooking and are mutagenic in the Ames Salmonella assay after metabolic activation by cytochrome P450. Studies with the HAA known as PhIP show that cynomolgus monkeys are able to metabolically activate it *in vivo*, resulting in DNA adducts that can be found in all tissues examined to date, including white blood cells. These metabolism studies suggest that PhIP may prove to be carcinogenic in nonhuman primates. In studies of the metabolism of HAAs in the mammary gland of rats, PhIP metabolites in breast milk have been identified and their potential role in mammary carcinogenesis is currently being assessed. HAAs may also be associated with cardiac abnormalities. Studies have shown that cynomolgus monkeys chronically treated with IQ had elevated levels of DNA adducts in the heart and developed foci of cardiac myocyte necrosis. Research efforts will continue to explore the various aspects of the metabolic activation of HAAs and their carcinogenic potential.

Division of Cancer Prevention, and Control

The American Stop Smoking Intervention Study (ASSIST) National 5-A-DAY Program

The National 5-A-DAY Program, designed to encourage Americans to eat five or more servings of fruits and vegetables every day, represents a significant public/private partnership between NCI and the Produce for Better Health Foundation. NCI's role in providing credible information plays an integral part in communicating the 5-A-DAY message. Research grants awarded to state health agencies, universities, and cancer centers are evaluating the effect of 5-A-DAY activities in schools, workplaces and other community settings.

Cancer in Minorities and the Underserved

Reducing cancer in minority and underserved populations is facilitated by the mobilization of professional and lay leaders in the community to address the specific cancer needs of that community as well as through coalition building among health-related, academic and community organizations. The NCI supports three such initiatives in an effort to address the cancer prevention and control needs of certain populations.

A major goal of the National Black Leadership Initiative on Cancer (NBLIC) is to address the barriers that limit or prevent Black Americans from gaining access to quality cancer control services. As of April 1994, the NBLIC has established 47

coalitions and is forming others in six regional areas of the U.S. The NBLIC recently established a collaborative working relationship with the American Association of Retired Persons (AARP) to plan and conduct more effective outreach programs targeting senior citizens.

The National Hispanic Leadership Initiative on Cancer (NHLIC) addresses cancer control barriers including risk factors, and cancer control service utilization in Hispanic communities. The NHLIC has established nine outreach sites involved in mobilizing community leaders to promote awareness and utilization of culturally sensitive and linguistically competent cancer prevention and control programs.

The third of these initiatives, the Appalachian Leadership Initiative on Cancer (ALIC) is a rural health initiative to establish community-based cancer prevention and control outreach programs for the medically underserved population in the Appalachian region of the United States. Among the ALIC's priorities are the promotion of smoking cessation, diet modification, and early detection screening and treatment. Measurable improvements are expected in this region in knowledge about prevention and early detection of cancer, and access and utilization of diagnostic and treatment services.

Cancer has become the leading cause of death for Alaskan Native women and the second leading cause of death among both Native American and Native Hawaiian women. The Native American Women's Cancer Initiative was developed in response to emerging cancer needs and issues of Native American women. Numerous barriers have been identified that interfere with cancer prevention and control efforts among indigenous women. In addition, the types and impact of such barriers vary among native communities in different regions of the country. Research projects focus on identifying barriers to culturally appropriate quality cancer control services and reducing cancer risk behaviors in Native American women.

Women's Health Trial: Feasibility Study in Minority Populations

NCI also has been exploring a dietary intervention, specifically fat restriction, to reduce the risk of developing breast, colorectal, and possibly cardiovascular diseases in postmenopausal women in the Women's Feasibility Study in Minority Populations. Approximately 2,250 women, 45 to 69 years of age have been enrolled to this multi-center randomized clinical trial. This study is testing methods to enable these women to modify their eating habits to a low-fat eating pattern as well as evaluating the impact of social customs, culture, and economic status on achieving and maintaining a dietary pattern that reduces fat intake. Elements of this trial have been used in the design and implementation of dietary interventions with the projected 10-year trans-NIH, multidisciplinary Women's Health Initiative, a national study of dietary modification, vitamin and mineral supplementation and hormonal replacement therapy in post-menopausal women.

National DES Educational Program for Health Professionals and the Public

NCI is sponsoring a cooperative agreement to develop, implement, and evaluate health education programs to inform DES exposed mothers, daughters, sons, and the health professionals who care for them about risks associated with DES exposure and of appropriate early detection, diagnosis and treatment strategies

for DES-related malignancies and other conditions. Diethylstilbestrol (DES) is a synthetic estrogen used to prevent miscarriages from the 1940s through 1971. DES was later found to be associated with an increased incidence of rare vaginal clear cell cancer in young women who had been DES exposed in utero. Mothers who were prescribed DES have also been found to have a 40 percent increased risk of breast cancer. A national education is now being conducted to test a regional breast cancer screening program for women exposed to DES. Members of existing cohorts of women exposed to DES as well as members of various DES action groups and callers to the CIS Hotline are being used to identify those eligible for screening.

Screening for Prostate, Lung, Colorectal, and Ovarian Cancers

The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) is a randomized, controlled clinical trial designed to determine whether particular screening modalities for prostate, lung, colorectum, and ovary will reduce the number of deaths through early detection of these cancers. Over the next eight years this trial will randomize 148,000 participants with equal numbers of men and women ages 60-74 years. Individuals in this age group are being asked to volunteer for the trial because the risk of these cancers is high in this age group. The 37,000 men randomized to the intervention arm of the study will have a yearly digital rectal examination and a blood test for prostate-specific antigen (PSA) for prostate cancer, an annual chest x-ray for lung cancer, and a flexible sigmoidoscopy at the initial visit and another three years later for colorectal cancer. Equal numbers of women in the intervention group will receive an annual chest x-ray, and a sigmoidoscopy at the initial visit and another three years later, for lung and colorectal cancers respectively. For ovarian cancer screening women will have an annual ovarian palpation, transvaginal ultrasound, and blood test for the tumor marker, CA-125. The pilot phase of the trial concluded in September of 1994 and a thorough evaluation of this phase will be completed in early 1995.

Prostate Cancer Prevention Trial with Finasteride

The Prostate Cancer Prevention Trial (PCPT) is being conducted in the CCOP clinical trials network. The trial is an intergroup study involving over 225 community and university hospitals across the country and is coordinated by the Southwest Oncology Group (SWOG). The study tests the ability of finasteride (Proscar), a 5-alpha-reductase inhibitor of androgen synthesis, to reduce the incidence of prostate cancer, the most common cancer in men.

The PCPT will include approximately 18,000 men from across the United States. Participation is open to all men between ages 55 and 70. Black men and men with a family history of prostate cancer are being aggressively recruited because they may have the greatest risk of developing prostate cancer. Men entering the study are randomized to receive finasteride or placebo for 7 years. The total trial will last 10 years. Prostate cancer will be detected during follow-up by physical examinations and blood tests and, at the end of the study, by prostate biopsy. The trial will also help determine the worth of annual prostate examinations and serial prostate-specific antigens (PSA) blood tests in detecting prostate cancers. The trial will provide the first biopsy-based characterization of the prevalence of occult prostate tumors in men over age 55.

Breast Cancer Prevention Trial with Tamoxifen

The Breast Cancer Prevention Trial (BCPT) with tamoxifen is currently underway in the CCOP clinical trials network. The trial is being conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and includes participants from over 300 centers across the U.S. and Canada with nearly 11,000 participants enrolled and randomized to either tamoxifen or placebo. The study tests the ability of tamoxifen, an anti-estrogen medication used in post-surgical treatment of early stage breast cancer, to prevent the development of breast cancer in women at increased risk for developing the disease. Approximately 16,000 women at increased risk for breast cancer due to various factors such as age, family history, and personal history (i.e., age at first birth, age at menarche, and previous breast biopsies) will be randomized to receive tamoxifen (20 mg/day) or placebo for a period of 5 years.

Community Clinical Oncology Program (CCOP)

The Community Clinical Oncology Program (CCOP) links community cancer specialists, primary care physicians, and other health care professionals to conduct both clinical treatment research and cancer prevention and control research studies. Research areas include: early detection and screening, chemoprevention, patient management, continuing care, and rehabilitation; testing intervention strategies such as chemoprevention in large populations; and assessing the impact of targeted research on community practices.

Through the network's access to cured cancer patients, their families, and other individuals at increased risk of developing cancer, NCI implements large-scale chemoprevention trials to study the effectiveness of various agents to prevent cancer. Examples include the Breast Cancer Prevention Trial (BCPT) with tamoxifen, and the Prostate Cancer Prevention Trial (PCPT) with finasteride.

The current program involves 48 community programs in 27 States with over 315 hospitals and 2,900 physicians. Annually, the CCOP enters approximately 4,000 patients onto treatment clinical trials, representing about one third of the annual accrual to NCI-approved randomized Phase III clinical trials.

Minority-Based Community Clinical Oncology Program (MBCCOP)

The Minority-Based Community Clinical Oncology Program (MBCCOP) is a network of community cancer specialists, primary care physicians and other health care professionals who conduct both clinical treatment research and cancer prevention and control research studies.

The MBCCOP provides a vehicle to develop and implement effective treatment and cancer control strategies in minority populations and allows for the study of minority recruitment and accrual to cancer clinical trials. This program was initiated to provide minority cancer patients with access to state-of-the-art cancer treatment and control technology. Ten programs with greater than 50 percent of new cancer patients from minority populations are currently funded.

**Division of
Extramural Activities**

Cancer Centers and Cancer Control in Minority Populations

The National Cancer Institute seeks to expand minority involvement in cancer control research, through the Comprehensive Minority Biomedical Program (CMBP) and the Cancer Center Minority Enhancement Awards (MEAs). MEAs are awarded competitively as supplements to NCI Cancer Centers for the purpose of facilitating the participation of minority groups in cancer control research. By broadening the operational base of cancer centers, MEAs allow expansion of center-based cancer control efforts in prevention, early detection, screening, pre-treatment evaluation, treatment, continuing care and rehabilitation, as well as stimulating the increased involvement of those primary care providers who serve minority populations. Three awards were made to institutions in prior years. An additional award was approved for funding in 1994.

The Minority Health Professional Training Initiative (MHPTI)

The MHPTI, which began in 1991, supports training and career development opportunities for minority health professionals by providing opportunities in oncology research and other subspecialties related to cancer. Such opportunities will increase the number of minority clinicians, clinical researchers, and other health professionals who are prepared to deal with the problem of excess mortality among minority populations due to cancer. Awards were made to minority clinicians in 1992 and 1993. Efforts are being made to expand this program.

Research Supplements for Underrepresented Minorities

The NIH-wide supplemental program "Initiatives for Underrepresented Minorities in Biomedical Research", began as an extension of the NCI Minority Investigator Supplement Program. This program provides supplemental funding to existing grants to fund participation of minorities in specific research projects. The targeted groups include for minority high school students, minority undergraduate students, minority graduate research assistants, minority individuals in postdoctoral training and minority staff or faculty. While this mechanism provides support indirectly to minority scientists and students by way of funded grantees, the ultimate intent of these awards is to influence a greater number of minority individuals to develop their research capabilities and pursue independent careers as cancer research investigators.

Co-funding

For the purpose of encouraging undergraduate and graduate students to pursue training related to cancer research, NCI co-funds, with the Minority Access to Research Careers (MARC) Program of National Institute of General Medical Sciences, pre-doctoral fellowships to minority students and Honors Undergraduate Training Grants to minority institutions. Similarly, through co-funding with the Minority Biomedical Research Support (MBRS) program, NCI provides support for specific cancer-related projects at participating minority institutions.

Through the High School Apprentice Program, the NCI contributed to the broadened involvement of high school researchers. Fifty awards were issued in 1994.

Other NCI Training Opportunities

The Summer Training Supplement is an extension of the MARC program and provides increased training opportunities for MARC scholars by way of short-term intramural laboratory training at the NCI.

Support for Meeting Attendance

CMBP continues to encourage participation of minority students and researchers in annual professional scientific meetings by providing travel support to such organizations as the American Association for Cancer Research and the Electron Microscope Society of America.

Cancer Information Dissemination

The CMBP, jointly with the Office of Cancer Communications (OCC), continues its efforts to heighten awareness about cancer risk and prevention in Black Americans. A contract solicitation was undertaken, and the published Request for Proposal (RFP) was targeted to the network of Black colleges and universities in a variety of settings with close ties to the Black community. The aim of this undertaking is to develop and disseminate information through educational programs regarding steps that can be taken to control or reduce cancer in Black Americans.

Office of the Director Health Communication Internship/Fellowship Program

To increase the number of persons trained in cancer communications, this program provides a variety of training experiences for graduate-level students in health communications. Fellows are located in various parts of the Office of Cancer Communications and the International Cancer Information Center, where they work with staff members on health education projects or science writing.

Cancer Information Service

The Office of Cancer Communications supports a nationwide network of offices known as the Cancer Information Service (CIS). The CIS serves as the NCI's primary mechanism to disseminate accurate up-to-date information to the American public at the community level. As OCC field offices, the CIS provides information on cancer and local resources through its toll free phone service.

Over 500,000 calls are received each year. In addition, the CIS serves as a catalyst for the adoption and adaptation of NCI education programs. Under a new program structure implemented in 1993, regional CIS offices now serve the entire continental United States, Alaska, Hawaii, and Puerto Rico. The CIS offices are funded through a contract mechanism with NCI designated cancer centers and community hospitals.

International Cancer Information Center

To increase the dissemination of cancer research and treatment information to physicians, researchers and other health professionals involved in cancer care, the International Cancer Information Center (ICIC) established the National Cancer Institute Information Associates Program, a membership service providing access to all of the NCI's scientific information products and services for health professionals through one point of contact and for one low yearly fee. Benefits of membership include a subscription to the *Journal of the National Cancer Institute* and copies of all *Journal of the National Cancer Institute*

Monographs; access to a toll-free dial-up Bulletin Board Service (BBS), which in turn provides access to the PDQ database, CANCERLIT Citation and Abstract Digests, Fact Sheets for Patients from the Office of Cancer Communications, and electronic mail and on-line conferences; Internet access to PDQ; and a toll-free member service line staffed with trained, bilingual representatives.

The ICIC has also been designated as a Public Health Service Reinvention Laboratory under Vice President Al Gore's National Performance Review. Designed to foster innovation in government, reinvention laboratories are areas within the federal government selected to demonstrate how re-engineering work processes, increasing delegations of authority, and empowering employees can improve efficiency and increase customer satisfaction.

The ICIC is also exploring ways to make its products and services available through Mosaic software on the World Wide Web. Mosaic enables users to access full-color photographs, video, and sound.

In conjunction with the Patient Education Section of the Office of Cancer Communications, the ICIC is co-directing the PDQ/PIF Demonstration Project, in which eight sites around the country will work to develop more effective ways to present and disseminate the patient information in PDQ. Phase I of the PDQ/PIF Project was completed last year.

Office Of International Affairs

OIA coordinates collaborative research between American and foreign scientists by cosponsoring international workshops and scientist exchanges. Fifteen workshops and 200 scientist exchanges were sponsored during 1994. Many more required no OIA funding. Eight European Organization for Research and Treatment of Cancer (EORTC) and ten Japanese Foundation for Cancer Research (JFCR) exchangees came to American laboratories. NCI also contributed toward the funding of over 100 short-term International Cancer Technology Transfer Fellowships (ICRETT), a program administered by the International Union Against Cancer (UICC). In addition, over 700 foreign scientists were at NCI under the NIH Visiting Program.

The Oncology Research Faculty Development Program for scientists from the developing world supported 16 trainees during 1994. A new program of Career Development Awards for Young Cancer Researchers in the newly independent states of the former USSR was begun in 1994. Awards have been made to scientists in Tallinn (Estonia), Riga (Latvia), Vilnius (Lithuania), Novosibirsk, Obninsk, and St. Petersburg (Russia), and Kiev (Ukraine).

A CD-ROM product containing the PDQ and CANCERLIT databases has been installed at over 50 cancer centers in Central and Eastern Europe, Latin America, the Caribbean, and developing Asian and African countries. Due to limitations inherent in this method of information dissemination, OIA is beginning a transition to alternative means of accessing cancer information through Internet electronic mail (e-mail).

OIA maintains liaison between the NCI and international agencies involved in cancer research and prevention, such as the EORTC, IARC, UICC, OECI, PAHO, WHO, and with national organizations which have international components, such as the American Cancer Society (ACS) and NAS in the U.S.; the United Kingdom Coordinating Committee for Cancer Research (UKCCCR), the Cancer Research Campaign (CRC), and Imperial Cancer Research Fund in the United Kingdom, the Association pour la Recherche sur le Cancer (ARC); Centre National de la Recherche Scientifique (CNRS), and Institut National de la Sante et de la Recherche Medicale (INSERM) in France; the JFCR, and the Japan Society for the Promotion of Science (JSPS); and many more.

Public Information Dissemination

As part of its legislated mission, the National Cancer Institute actively supports cancer information dissemination activities. NCI works to ensure that the public, including patient, and health professionals, are afforded easy access to up-to-date information regarding cancer prevention, detection and diagnosis, and treatment measures.

The NCI's information dissemination efforts include behavior modification interventions, such as smoking cessation and breast cancer screening, as well as education activities specifically directed towards professional, public, and patient audiences. The PDQ system is a database containing treatment recommendations and summary information on all active clinical trials supported by NCI. A directory of physicians and organizations that provide cancer care is also included in the PDQ system.

The Cancer Information Service, accessible to the public by dialing 1-800-4-CANCER, is staffed by information specialists equipped to respond to public inquiries regarding cancer; often the PDQ system will be consulted. Over one-half of the callers receive a publication or other written material as a result of this service. Heightened public interest in new cancer treatment (i.e., gene therapy, taxol), results in a flood of calls to this toll-free number.

The Cancer Information Service consists of a nationwide network of 19 regional offices. In addition to providing direct response to the public, the field offices support NCI's major outreach activities and conduct cancer education programs to meet specific local and regional needs.

In addition to individual mailings of pamphlets/brochures by the local network offices, the NCI widely distributes bulk volumes of pamphlets/brochures to hospitals, supermarkets, physician organizations, etc., for subsequent distribution to the public.

| Pamphlets/Brochures Distributed | | | | |
|---------------------------------|------------------|----------------------------------|------------------------------------|-----------------|
| | CIS Inquiries | Publication Ordering Calls | Total Literature Distributed | PDQ Searches |
| 1994 | 600,000 | 200,000 | 25,000,000 | 30,000 |

Scientific Information Dissemination

The International Cancer Information Center continues to promote the use of its products and services to the widest audiences possible, primarily through the NCI Information Associates Program, and also through its individual electronic products and services. PDQ's Treatment, Supportive Care, Screening and Prevention, and Drug Information Statements, along with Fact Sheets on various cancer-related topics, Search Citations and Abstracts from the CANCERLIT database, and news items, are available via fax through CancerFax® and via Internet electronic mail through CancerNet™. Many of these items are also available on gopher servers around the world.

The *Journal of the National Cancer Institute*, the NCI's peer-reviewed scientific journal, continues to provide information regarding clinical and basic research advances to cancer professionals worldwide. Journal articles are currently the most frequently cited out of 78 oncology journals worldwide.

The ICIC continues to promote the Information Associates Program and the other scientific information services for health professionals at national and international medical meetings.

Directory of Personnel

Director, National Cancer Institute

| | | | |
|---|--------------------------|---------------------|--------------|
| | Dr. Samuel Broder | Building 31 11-A-48 | 301-496-5615 |
| <i>Acting Deputy Director</i> | | | |
| | Dr. Edward J. Sondik | Building 31 11-A-48 | 301-496-1927 |
| <i>Assistant Director for Applied Science</i> | | | |
| | Dr. Judith E. Karp | Building 31 11-A-27 | 301-496-3505 |
| <i>Program Manager, Equal Employment Opportunity Office</i> | | | |
| | Ms. Maxine I. Richardson | Building 31 10-A-33 | 301-496-6266 |
| <i>Director, Office of Legislation and Congressional Activities</i> | | | |
| | Ms. Dorothy Tisevich | Building 31 11-A-23 | 301-496-5217 |

Assistant Director for Program Operations and Planning

| | | | |
|---|--------------------|---------------------|--------------|
| | Ms. Iris Schneider | Building 31 11-A-48 | 301-496-5534 |
| <i>Chief, Planning, Evaluation, and Analysis Branch</i> | | | |
| | Ms. Cherie Nichols | Building 31 11-A-21 | 301-496-5515 |

Acting Associate Director for Cancer Prevention Research Program

| | | | |
|--|---------------------|---------------------|--------------|
| | Dr. Peter Greenwald | Building 31 10-A-52 | 301-496-6616 |
|--|---------------------|---------------------|--------------|

Associate Director for Cancer Communications

| | | | |
|---|-----------------------|---------------------|--------------|
| | Mr. J. Paul Van Nevel | Building 31 10-A-31 | 301-496-6631 |
| <i>Chief, Information Resources Branch</i> | | | |
| | Ms. Nancy Brun | Building 31 10-A-30 | 301-496-4394 |
| <i>Acting Chief, Reports and Inquiries Branch</i> | | | |
| | Mr. J. Paul Van Nevel | Building 31 10-A-31 | 301-496-6631 |
| <i>Acting Chief, Information Projects Branch</i> | | | |
| | Ms. Ruth Mattingly | Building 31 10-A-03 | 301-496-6667 |

Associate Director for International Affairs

| | | | |
|--|---------------------|--------------------|--------------|
| | Dr. Federico Welsch | Building 31 4-B-55 | 301-496-4761 |
|--|---------------------|--------------------|--------------|

Associate Director for International Cancer Information Center

| | | | |
|--|------------------------|-----------------|--------------|
| | Ms. Susan M. Hubbard | Building 82 102 | 301-496-9096 |
| <i>Chief, Computer Communications Branch</i> | | | |
| | Mr. Nicholas B. Martin | Building 82 219 | 301-496-8880 |
| <i>Chief, Scientific Publications Branch</i> | | | |
| <i>Managing Editor, Journal of the National Cancer Institute</i> | | | |
| | Ms. Julianne Chappell | Building 82 235 | 301-496-1997 |
| <i>Chief, International Cancer Research Data Bank Branch</i> | | | |
| | Dr. Gisele Sarosy | Building 82 113 | 301-496-7406 |

| | | |
|--|---------------------------|----------------------------------|
| <i>Associate Director for Administrative Management</i> | | |
| Mr. Philip D. Amoruso | Building 31 11-A-48 | 301-496-5737 |
| <i>Deputy Associate Director for Administrative Management</i> | | |
| Mr. Donald Christoferson | Building 31 11-A-48 | 301-496-5737 |
| <i>Chief, Administrative Services Branch</i> | | |
| Ms. Susan Kiser | Building 31 11-A-33 | 301-496-5801 |
| <i>Chief, Financial Management Branch</i> | | |
| Mr. John P. Hartinger | Building 31 11-A-16 | 301-496-5803 |
| <i>Chief, Personnel Management Branch</i> | | |
| Ms. Marianne Wagner | Building 31 3-A-19 | 301-496-3337 |
| <i>Chief, Research Contracts Branch</i> | | |
| Mr. John P. Campbell, Jr. | Executive Plaza South 604 | 301-496-8628 |
| <i>Chief, Management Analysis Branch</i> | | |
| Ms. Marilyn Jackson | Executive Plaza South 550 | 301-496-6985 |
| <i>Chief, Grants Administration Branch</i> | | |
| Mr. Leo F. Buscher, Jr. | Executive Plaza South 234 | 301-496-7753 |
| <i>Chief, Extramural Financial Data Branch</i> | | |
| Mr. Stephen M. Hazen | Executive Plaza South 643 | 301-496-7660 |
| <i>Chief, Management Information Systems Branch</i> | | |
| Ms. Betty Ann Sullivan | Executive Plaza South 511 | 301-496-1038 |
| | | |
| <i>Acting Director, Office of Laboratory Animal Science</i> | | |
| Dr. Patricia Brown | Building 31 4-B-59 | 301-496-1866 |
| | | |
| <i>Director, Office of Technology Development</i> | | |
| Dr. Thomas D. Mays | Building 31 4-A-51 | 301-496-0477 |
| | | |
| <i>Associate Director for Frederick Cancer Research and Development Center</i> | | |
| Frederick Cancer Research and Development Center, Frederick Maryland | | |
| <i>Director</i> | Dr. Jerry Rice | Building 427 9 8-301-846-5096 |
| | | |
| <i>General Manager/Project Officer</i> | | |
| Dr. Cedric W. Long | Building 427 8 | 8-301-846-1108 |
| | | |
| <i>Deputy General Manager</i> | | |
| Mr. Richard Carter | Building 427 3 | 8-301-846-1106 |
| | | |
| <i>Acting Director, Division of Cancer Etiology</i> | | |
| Dr. Jerry Rice | Building 31 11-A-03 | 301-496-6618 |
| | | |
| <i>Acting Administrative Officer</i> | | |
| Ms. Virginia Kiesewetter | Building 31 11-A-11 | 301-496-6556 |

| | | | |
|---|--------------------------|---------------------------|--------------|
| <i>Director, Division of Cancer Biology, Diagnosis, and Centers</i> | | | |
| | Dr. Alan S. Rabson | Building 31 3-A-11 | 301-496-4345 |
| <i>Administrative Officer</i> | | | |
| | Mr. Lawrence D. Willhite | Building 31 3-A-11 | 301-496-3381 |
| | | | |
| <i>Director, Division of Cancer Treatment</i> | | | |
| | Dr. Bruce A. Chabner | Building 31 3-A-44 | 301-496-4291 |
| <i>Administrative Officer</i> | | | |
| | Mr. Lawrence J. Ray | Building 31 3-A-44 | 301-496-2775 |
| | | | |
| <i>Director, Division of Extramural Activities</i> | | | |
| | Dr. Marvin Kalt | Executive Plaza North 600 | 301-496-5147 |
| <i>Administrative Officer</i> | | | |
| | Ms. Deborah Jarman | Executive Plaza North 604 | 301-496-5915 |
| | | | |
| <i>Director, Division of Cancer Prevention and Control</i> | | | |
| | Dr. Peter Greenwald | Building 31 10-A-52 | 301-496-6616 |
| <i>Administrative Officer</i> | | | |
| | Mr. Nicholas Olimpio | Building 31 10-A-50 | 301-496-9606 |

Former Directors of the National Cancer Institute

Dr. Vincent T. DeVita, Jr., M.D.
January 1980 - June 1980 (Acting)
July 1980 - August 1988

Dr. DeVita joined NCI in 1963 as a Clinical Associate in the Laboratory of Chemical Pharmacology. He served NCI as head of the Solid Tumor Service, Chief of the Medicine Branch, Director of the Division of Cancer Treatment and Clinical Director prior to his appointment as Director of NCI.

Dr. Arthur Canfield Upton, M.D.
July 1977 - December 1979

Prior to his tenure as NCI Director, Dr. Upton served as Dean of the School of Basic Health Sciences at the State University of New York at Stony Brook.

Dr. Frank Joseph Rauscher, Jr., Ph.D.
May 1972 - October 1976

Dr. Rauscher served as Scientific Director for Etiology, NCI, prior to his appointment as Director of NCI in 1972.

Dr. Carl Gwin Baker, M.D.
November 1969 - July 1970 (Acting)
July 1970 - April 1972

During his tenure with PHS, Dr. Baker served as Scientific Director for Etiology, NCI, and as Acting Director of NCI prior to his appointment as Director in July 1970.

Dr. Kenneth Milo Endicott, M.D.
July 1960 - November 1969

Dr. Endicott served as Chief of the Cancer Chemotherapy National Service Center, PHS, and as Associate Director, NIH, prior to being appointed Director, NCI in July 1960.

Dr. John Roderick Heller, M.D.
May 1948 - June 1960

Dr. Heller joined PHS in 1934 and became Chief of the Venereal Disease Division prior to his appointment as Director of NCI in 1948.

Dr. Leonard Andrew Scheele, M.D.
July 1947 - April 1948

Dr. Scheele served in various capacities during his tenure with PHS prior to his appointment as Assistant Chief and, subsequently, Director of NCI in July 1947.

Dr. Roscoe Roy Spencer, M.D.
August 1943 - July 1947

Dr. Spencer became NCI's first Assistant Chief and, subsequently, was appointed Director of the Institute in 1943.

Dr. Carl Voegtlin, Ph.D.
January 1938 - July 1943

Dr. Voegtlin served as Professor of Pharmacology and Chief of the Division of Pharmacy at the Hygienic Laboratory prior to becoming the first Director of NCI in 1938.

National Cancer Advisory Board

| Appointees | Expiration of Appointment | Appointees | Expiration of Appointment | Appointees | Expiration of Appointment |
|---|---------------------------|---|---------------------------|--|---------------------------|
| Mrs. Barbara K. Rimer, Dr.P.H. Chairperson Duke University Durham, NC | 2000 | Pelayo Correa, M.D. Louisiana State University Medical Center New Orleans, Louisiana | 1998 | Sydney Salmon, M.D. Arizona Cancer Center Tucson, AZ | 1996 |
| Frederick F. Becker, M.D. University of Texas Houston, TX | 1996 | Robert W. Day, M.D., MPH, Ph.D Fred Hutchinson Cancer Research Center Seattle, Washington | 1998 | Philip S. Schein, M.D. U.S. Bioscience, Inc. West Conshohocken, PA | 2000 |
| J. Michael Bishop, M.D. The George Williams Hopper Research Foundation San Francisco, CA | 2000 | Mrs. Barbara P. Gimbel The Society of Memorial Sloan- Kettering Cancer Center New York, New York | 1998 | Ellen V. Sigal, Ph.D SIGAL Environmental Inc. Washington, D.C. | 1998 |
| Mrs. Zora K. Brown Cancer Awareness Program Washington, D.C. | 1998 | Alfred L. Goldson, M.D., F.A.C.A.R. Howard University Hospital Washington, D.C. | 2000 | Vainuts K. Vaitkevicius, M.D. Michigan Cancer Foundation Detroit, MI | 2000 |
| Paul Calabresi, M.D., Rhode Island Hospital Providence, RI | 1996 | Mrs. Marlene A. Malek Vincent Lombardi Cancer Center McLean, VA | 1996 | Charles B. Wilson, M.D. Brain Tumor Research Center U.C.S.F. San Francisco, Ca. | 1998 |
| Kenneth Chan, Ph.D Ohio State University Columbus, Ohio | 1996 | Deborah K. Mayer, R.N., M.S.N. Ontario Cancer Institute Toronto, Canada | 1996 | Executive Secretary Marvin R. Kalt, Ph. D. National Cancer Institute Bethesda, MD 20892 | |

EX OFFICIO MEMBERS

| | | |
|---|---|---|
| The Honorable Donna E. Shalala, Ph.D Secretary for Health and Human Services Washington, D.C. | Kenneth W. Kizer, M.D.M.P.H. Department of Veterans' Affairs Washington, D.C. | Ann Brown Consumer Product Safety Commission Bethesda, MD |
| Harold Varmus, M.D. Director, National Institutes of Health Bethesda, MD | David A. Kessler, M.D. Food and Drug Administration Rockville, MD | Kenneth Olden, M.D. National Institute of Environmental Health Sciences Research Triangle Park, NC |
| The Honorable Robert B. Reich Secretary of Labor Washington, D.C. | Linda Rosenstock, M.D., M.P.H. NIOSH Washington, D.C. | Rachel Levinson, Ph.D. Office of Science and Technology Policy Washington, D.C. |
| The Honorable Edward Martin, M.D. Acting Assistant Secretary of Defense Washington, D.C. | Ari Patrinos, Ph.D. Department of Energy Washington, D.C. | Carol M. Browner Environmental Protection Agency Washington, D.C. |

Alternates to Ex Officio Members

| | | |
|--|---|--|
| Marilyn A. Fingerhut, Ph.D. NIOSH Washington, D.C. | Hugh McKinnon, M.D. Environmental Protection Agency Washington, D.C. | Ralph E. Yodaiken, M.D. Department of Labor Washington, D.C. |
| John R. Johnson, M.D. Food and Drug Administration Rockville, MD | Raymond L. Sphar, M.D. Department of Veterans' Affairs Washington, D.C. | Captain Bimal C. Ghosh, M.D. Department of the Navy Washington, D.C. |
| | Andrew Ulsamer, Ph.D. Consumer Product Safety Commission Bethesda, MD | John C. Wooley, Ph.D. Department of Energy Washington, D.C. |

Division Boards of Scientific Counselors

| | | | | |
|---|--|--|--|---|
| Division of Cancer Biology, Diagnosis, and Centers | Robert L. Reddick, M.D. Chairperson | 1995 | Stanley J. Korsmeyer, Jr., M.D. Michael E. Lamm, M.D. | 1998 1997 |
| | Martin D. Abeloff, M.D. | 1995 | David M. Livingston, M.D. | 1996 |
| | Barbara F. Atkinson, M.D. | 1995 | Sue Ellen Martin, M.D., Ph.D. | 1997 |
| | Esther H. Chang, Ph.D. | 1996 | Ruth McCorkle, Ph.D. | 1998 |
| | Albert E. Dahlberg, M.D., Ph.D. | 1996 | Azorides R. Morales, M.D. | 1995 |
| | William F. Dove, Ph.D. | 1998 | Curtis L. Parker, Ph.D. | 1997 |
| | Lois B. Epstein, M.D. | 1995 | Alan Solomon, M.D. | 1996 |
| | Max E. Gottesman, M.D. | 1996 | Jouni Uitto, M.D., Ph.D. | 1996 |
| | Division of Cancer Treatment | Clara D. Bloomfield, M.D. Chairperson | 1995 | Barbara J. McNeil, M.D., Ph.D. Beverly S. Mitchell, M.D. |
| William R. Brody, M.D., Ph.D. | | 1998 | Rodrique Mortel, M.D. | 1995 |
| Charles A. Coltman, Jr., M.D. | | 1997 | Allen I. Oliff, M.D. | 1996 |
| Phillip Crews, Ph.D. | | 1994 | Lester J. Peters, M.D. | 1995 |
| Carlo M. Croce, M.D. | | 1995 | Ralph A. Reisfeld, Ph.D. | 1998 |
| Stephen H. Friend, M.D., Ph. D. | | 1998 | Anna Marie Skalka, Ph.D. | 1998 |
| Zvi Y. Fuks, M.D. | | 1997 | Paul M. Sondel, M.D., Ph.D. | 1997 |
| Philip D. Greenberg, M.D. | | 1996 | Glenn D. Steele, Jr., M.D., Ph.D. | 1995 |
| Sidney M. Hecht, Ph.D. | | 1997 | Wendell Wierenga, Ph.D. | 1998 |
| Division of Cancer Etiology | G. Barry Pierce, M.D. Chairperson | 1994 | Nancy E. Mueller, S.D. | 1997 |
| | Donald S. Davies, Ph.D. | 1995 | Nancy L. Oleinick, Ph.D. | 1995 |
| | Virginia L. Ernster, Ph.D. | 1997 | Alan P. Poland, M.D. | 1995 |
| | Stephen S. Hecht, Ph.D. | 1993 | Herman A. Schut, Ph.D. | 1998 |
| | Maurice R. Hilleman, Ph.D. | 1993 | James Swenberg, D.V.M., Ph.D. | 1997 |
| | Ru Chih C. Huang, Ph.D. | 1994 | Mimi C. Yu, Ph.D. | 1994 |
| | Division of Cancer Prevention and Control | Arnold D. Kaluzny, Ph.D. Chairperson | 1995 | Cutberto Garza, M.D., Ph.D. |
| John G. Boyce, M.D. | | 1996 | E. Robert Greenberg, M.D. | 1995 |
| Helene G. Brown | | 1995 | Melvin R. Moore | 1997 |
| David L. DeMets, Ph.D. | | 1997 | G. Marie Swanson, Ph.D., M.P.H. | 1996 |
| Eric R. Fearon, M.D., Ph.D. | | 1996 | Ian M. Thompson, Jr., M.D. | 1996 |
| Suzanne W. Fletcher, M.D. | | 1997 | Melvyn S. Tockman, M.D., Ph.D. | 1996 |
| Frederick Cancer Research and Development Center | | Donald R. Helinski, Ph.D. Chairperson | 1994 | Raymond L. Erikson, Ph.D. John M. Essigmann, Ph.D. |
| | John N. Abelson, Ph.D. | 1996 | Rasika M. Harshey, Ph.D. | 1996 |
| | Arnold J. Berk, M.D. | 1997 | John E. Johnson, Ph.D. | 1997 |
| | John M. Coffin, Ph.D. | 1996 | James L. Sherley, M.D., Ph.D. | 1996 |
| | Frank Costantini, Ph.D. | 1997 | Colin L. Stewart, D. Phil. | 1998 |
| | Elizabeth A. Craig, Ph.D. | 1998 | Susan S. Taylor, Ph.D. | 1998 |

President's Cancer Panel

Harold Freeman, M.D. 1994
Chairman
Director of Surgery
Harlem Hospital Center
New York, NY

Frances M. Visco, Esq. 1996
President
National Breast Cancer Coalition
Philadelphia, Pa.

Henry C. Pitot., M.D., Ph.D. 1995
Professor of Oncology and Pathology
McArdle Laboratory
University of Madison
Madison, Wisconsin

Executive Secretary
Maureen O. Wilson, Ph.D.
Assistant Director
National Cancer Institute
Building 31, Room 4A34
Bethesda, MD 20892

Executive Committee Members

Dr. Samuel Broder
Director

Dr. Edward J. Sondik
Acting Deputy Director

Mr. Philip D. Amoruso
Associate Director for Administrative
Management

Dr. Jerry Rice
Acting Director, Division of Cancer Etiology

Dr. Marvin A. Kalt
Director, Division of Extramural
Activities

Dr. Bruce A. Chabner
Director, Division of Cancer Treatment

Dr. Peter Greenwald
Director, Division of Cancer Prevention and Control

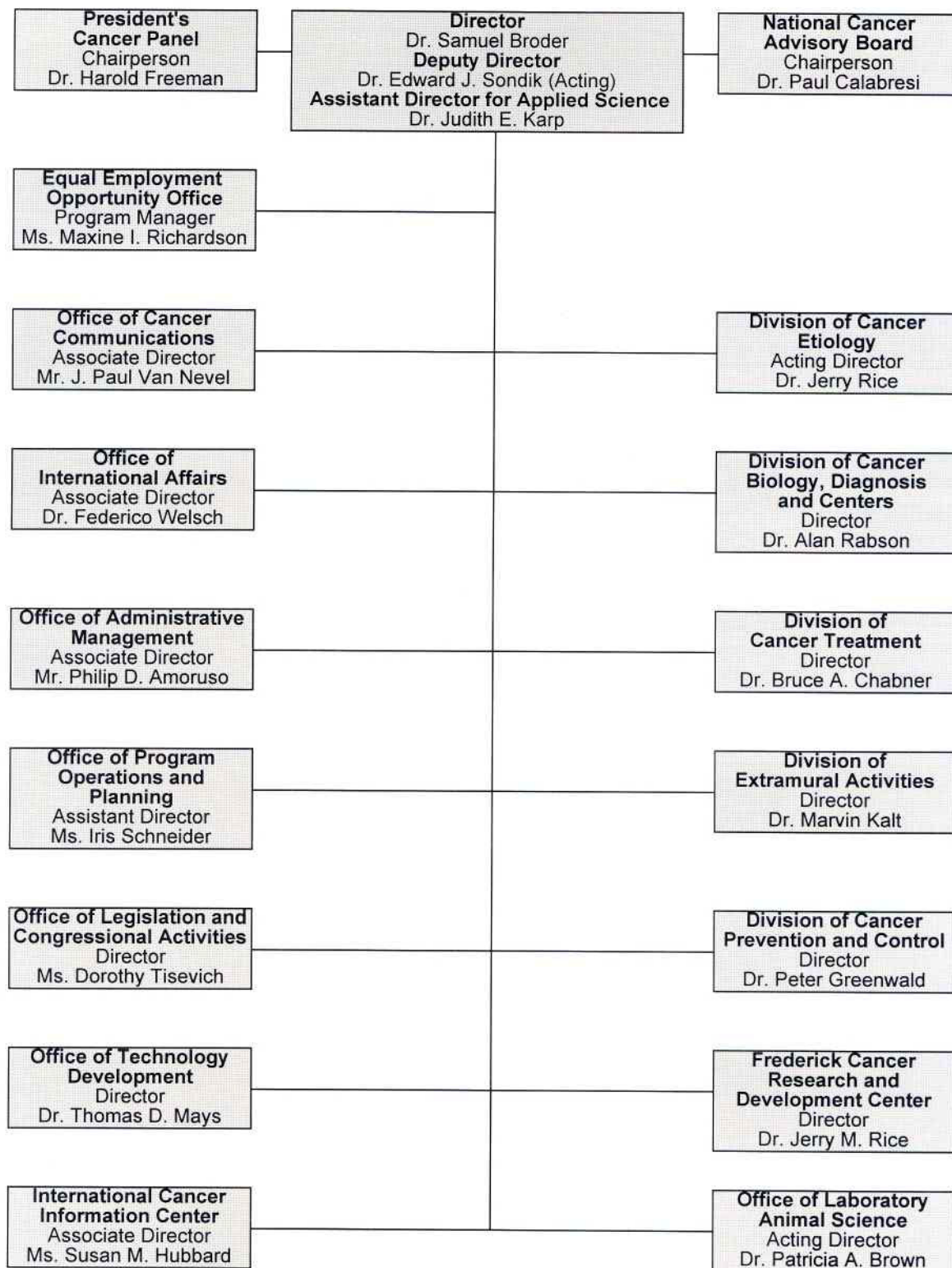
Dr. Jerry Rice
Associate Director, Frederick Cancer Research
and Development Center

Dr. Alan Rabson
Director, Division of Cancer Biology, Diagnosis and
Centers

Dr. Judith E. Karp
Assistant Director for Applied Science

Ms. Iris Schneider
Executive Secretary

National Cancer Institute Organization



Office of the Director

Dr. Samuel Broder, Director
Dr. Edward J. Sondik, Acting Deputy Director
Dr. Judith E. Karp, Assistant Director for Applied Science

(1) Serves as the focal point for the National Cancer Program; (2) Develops a National Cancer Plan; and monitors implementation of the Plan; (3) Directs and coordinates the Institute's programs and activities, and (4) Develops and provides policy guidance and staff direction to the Institute's programs in areas such as program coordination, program planning, clinical care and administrative management

Office of Legislation & Congressional Activities
Director
 Ms. Dorothy Tisevich

EEO Office
 Ms. Maxine I. Richardson

Office of Cancer Communications
 Mr. J. Paul Van Nevel

Office of International Affairs
 Dr. Federico Welsch

Office of Administrative Management
 Mr. Philip D. Amoroso

Office of Program Operations and Planning
 Ms. Iris Schneider

Office of Technology Development
 Dr. Thomas D. Mays

Office of Laboratory Animal Science
 Dr. Patricia A. Brown
 (Acting)

International Cancer Information Center
 Ms. Susan M. Hubbard

Information Resources Branch
 Ms. Nancy Brun

Reports and Inquiries Branch
 Mr. J. Paul Van Nevel
 (Acting)

Information Projects Branch
 Ms. Ruth E. Mattingly
 (Acting)

Administrative Services Branch
 Ms. Susan M. Kiser

Personnel Management Branch
 Ms. Marianne Wagner

Financial Management Branch
 Mr. John P. Hartinger

Research Contracts Branch
 Mr. John P. Campbell, Jr.

Grants Administration Branch
 Mr. Leo F. Buscher, Jr.

Management Analysis Branch
 Ms. Marilyn Jackson

Management Information Systems Branch
 Ms. Betty A. Sullivan

Extramural Financial Data Branch
 Mr. Stephen M. Hazen

Planning, Evaluation and Analysis Branch
 Ms. Cherie Nichols

Computer Communications Branch
 Mr. Nicholas B. Martin

Scientific Publications Branch
 Ms. Julianne Chappell

International Cancer Research Data Bank Branch
 Dr. Gisele Sarosy

Division of Cancer Biology, Diagnosis and Centers

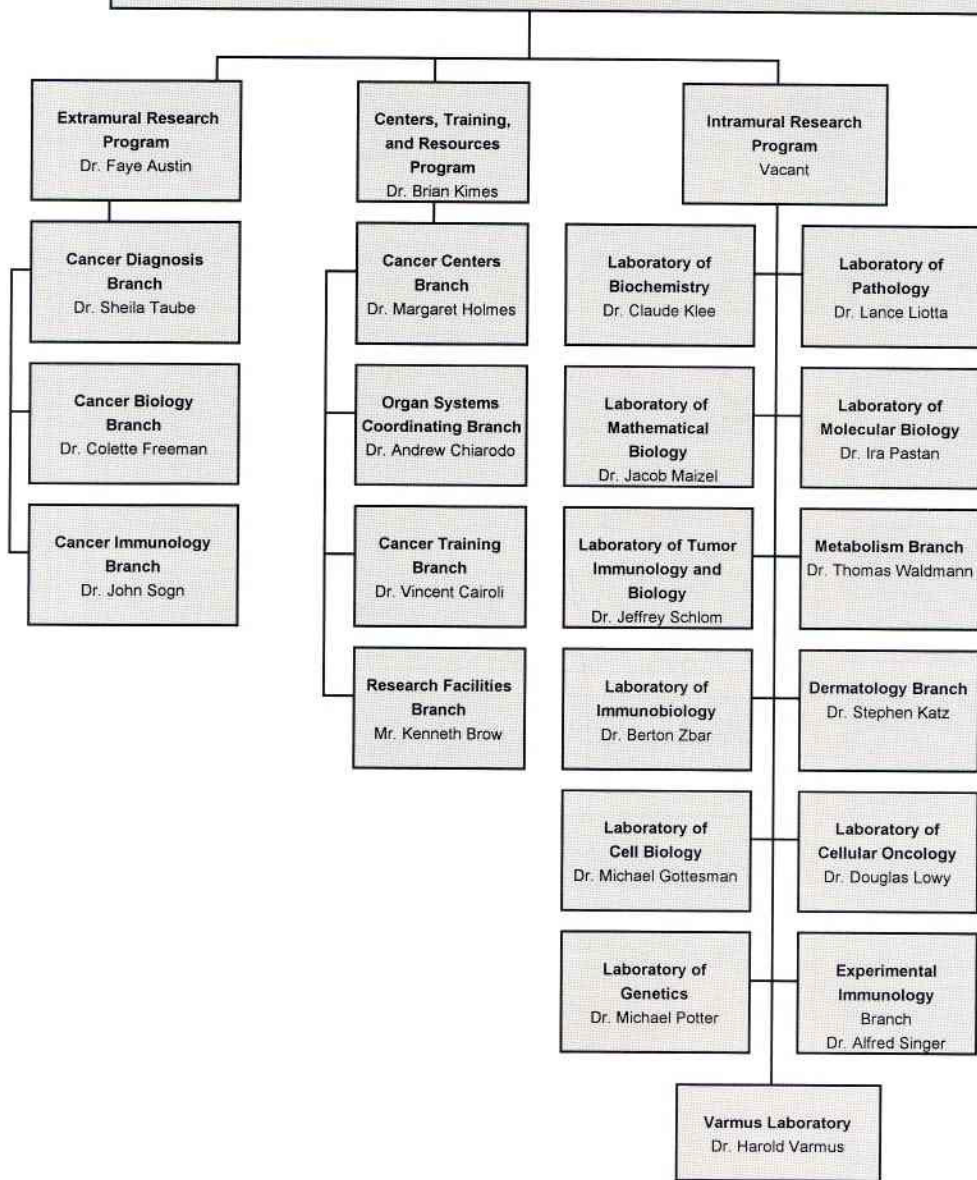
Dr. Alan S. Rabson, Director
Dr. Ihor J. Masnyk, Deputy Director

(1) Plans and directs the research activities of the National Cancer Institute relating to cancer biology and research in cancer biology and diagnosis; (3) Plans, directs, and coordinates an extramural program of basic and applied research conducted at cancer centers; (4) Plans and administers an extramural program which supports and fosters cancer research training, cancer clinical education, and cancer research career development in order to assure the continuing existence of a national cadre of highly qualified individuals to work in the fields of cancer research, treatment, and control; and (5) Administers a program of support for the construction, alteration, renovation, and equipping of extramural research facilities which house or will house cancer research and/or treatment activities.

Board of Scientific Counselors
 Dr. Robert L. Reddick

Planning and Analysis Branch
 Ms. Susan Waldrop

Administrative Management Branch
 Mr. Lawrence D. Willhite



Division of Cancer Treatment

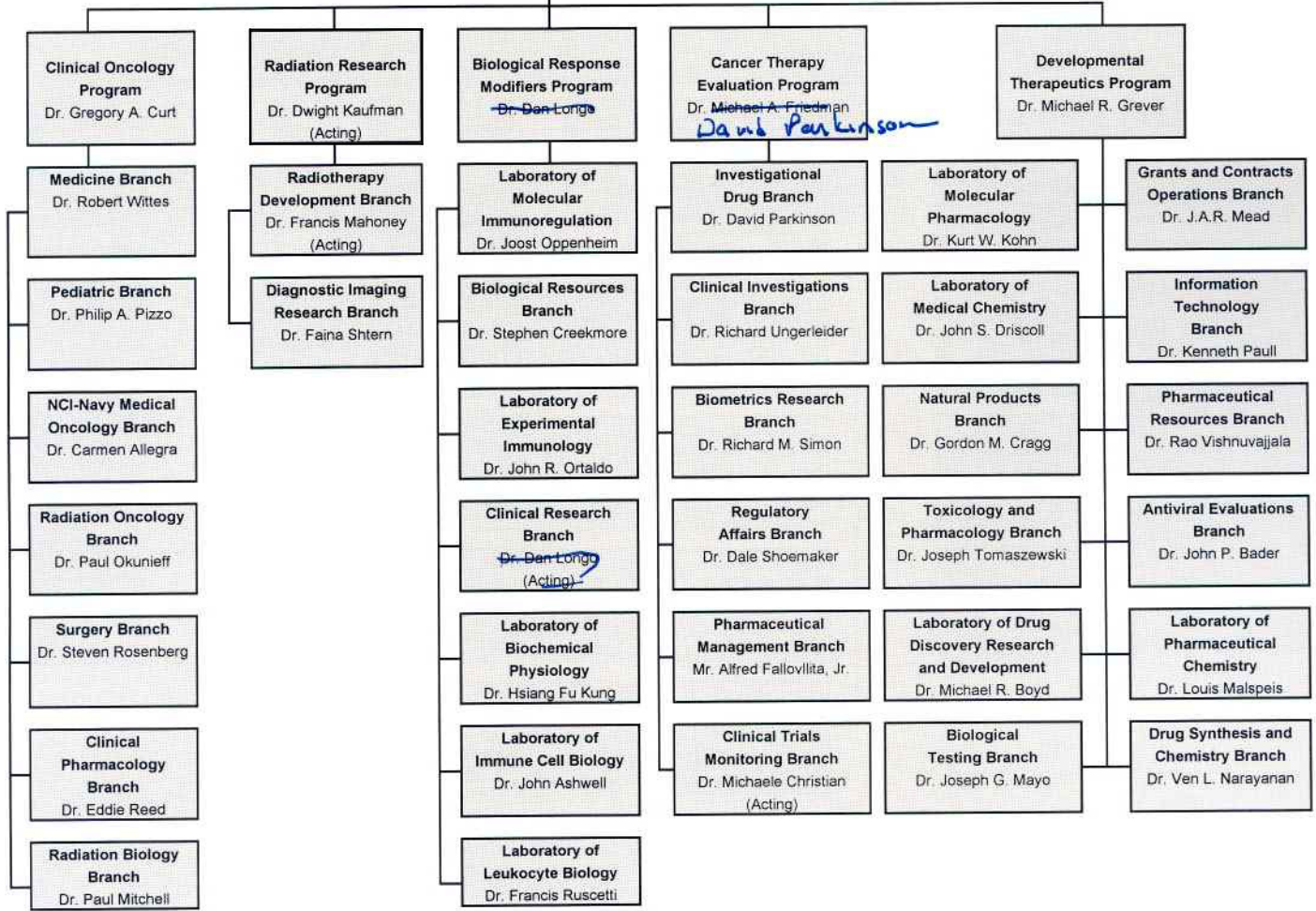
Robert Wittes
~~Dr. Bruce Chabner, Director~~

Dr. Dwight Kaufman, Deputy Director

Administrative Management and Planning Branch
 Mr. Lawrence J. Ray

Board of Scientific Counselors
 Chairperson
 Dr. Clara D. Bloomfield

(1) Plans, directs and coordinates an integrated program of intramural and extramural preclinical and clinical cancer treatment research as well as research conducted in cooperation with other Federal agencies with the objective of curing or controlling human cancer by utilizing treatment modalities singly or in combination; (2) Administers targeted research and development programs in areas of drug development, biological response modifiers and radiotherapy development; and (3) Serves as the national focal point for information and data on experimental and clinical studies related to cancer treatment and for the distribution of such information to appropriate scientists and physicians.



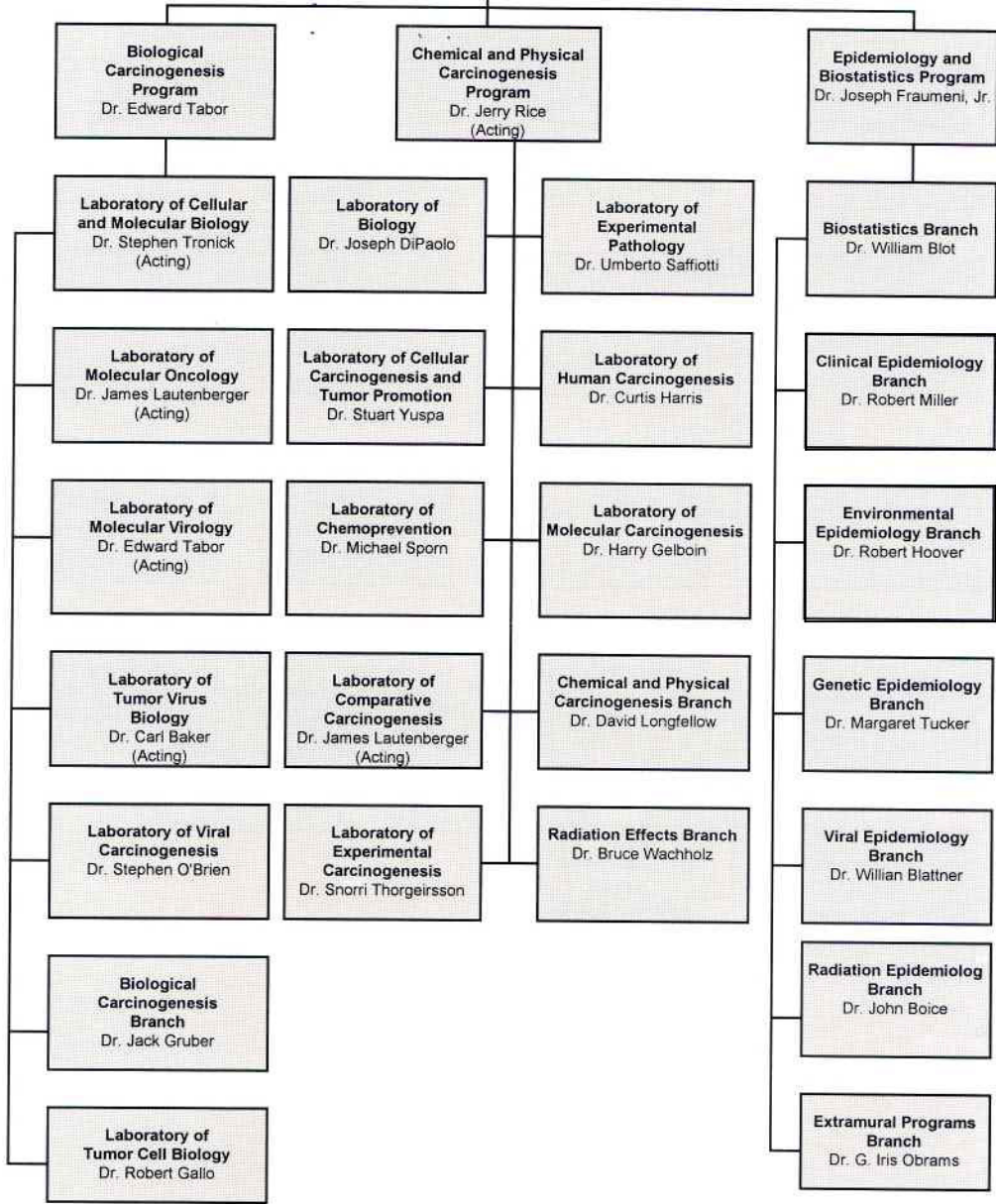
Division of Cancer Etiology

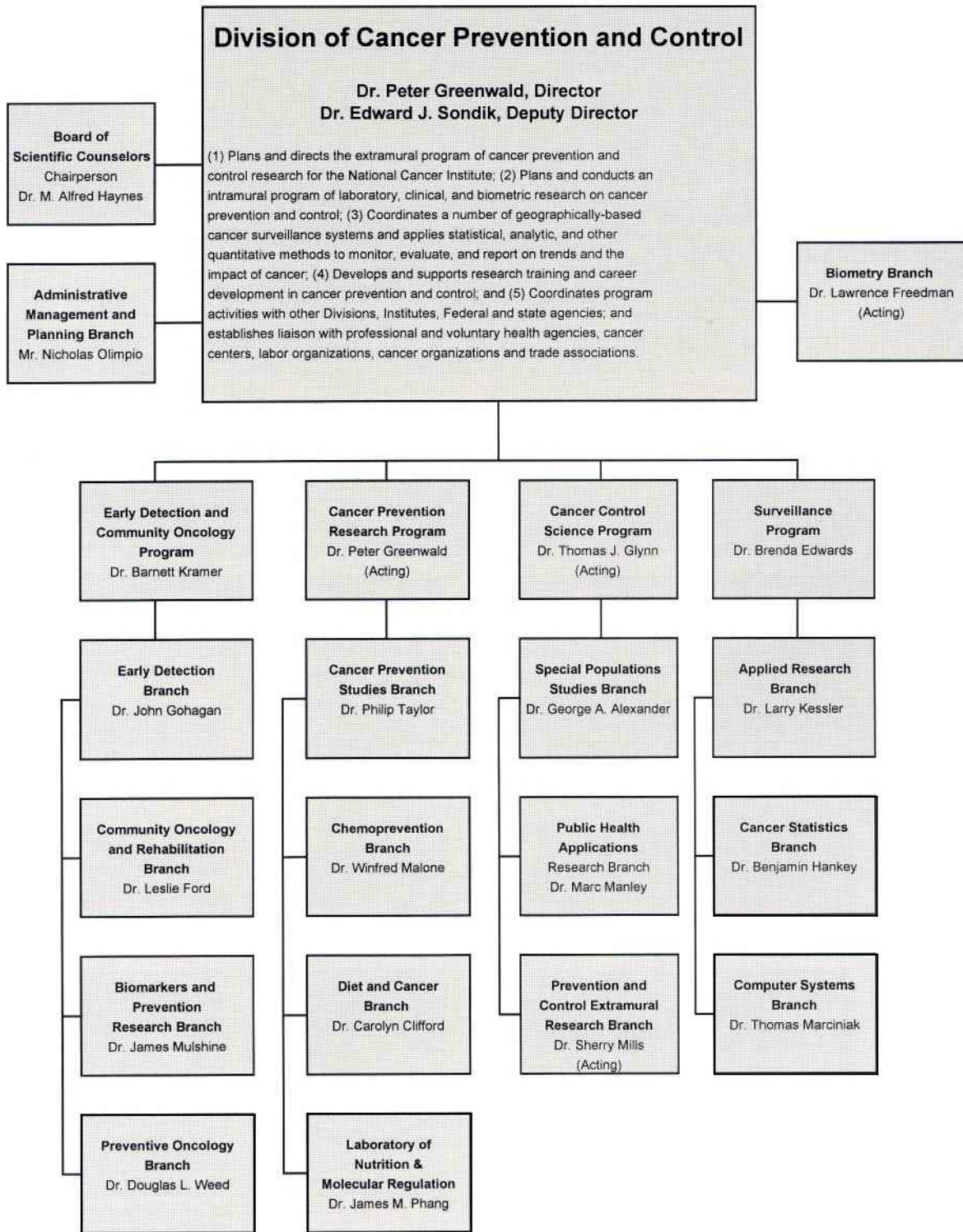
Dr. Jerry Rice, Acting Director
Dr. Susan Sieber, Deputy Director

Administrative Management Branch
Ms. Virginia Kieseewetter
(Acting)

(1) Plans and directs a national program of basic research including laboratory, field and epidemiologic and biometric research on the cause and natural history of cancer and means for preventing cancer. This program is implemented by intramural research, research grants, cooperative agreements, and contracts; (2) Evaluates mechanisms of cancer induction and promotion by chemicals, viruses and environmental agents; (3) Serves as the focal point for the Federal Government on the synthesis of clinical, epidemiological, and experimental data relating to cancer causation; and (4) Participates in the evaluation of, and advises the Institute Director on program related aspects of other basic research activities as they relate to cancer cause and prevention.

Board of Scientific Counselors
Chairperson
Dr. G. Barry Pierce

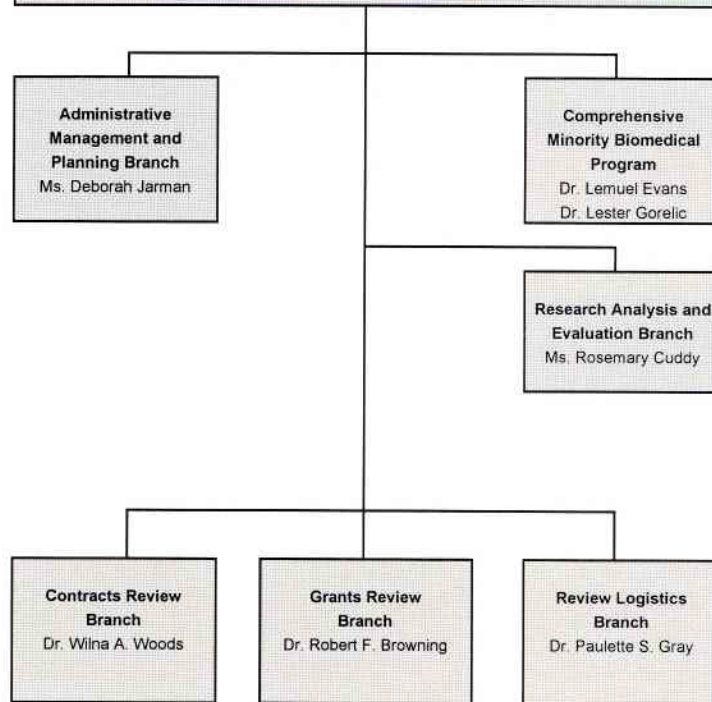




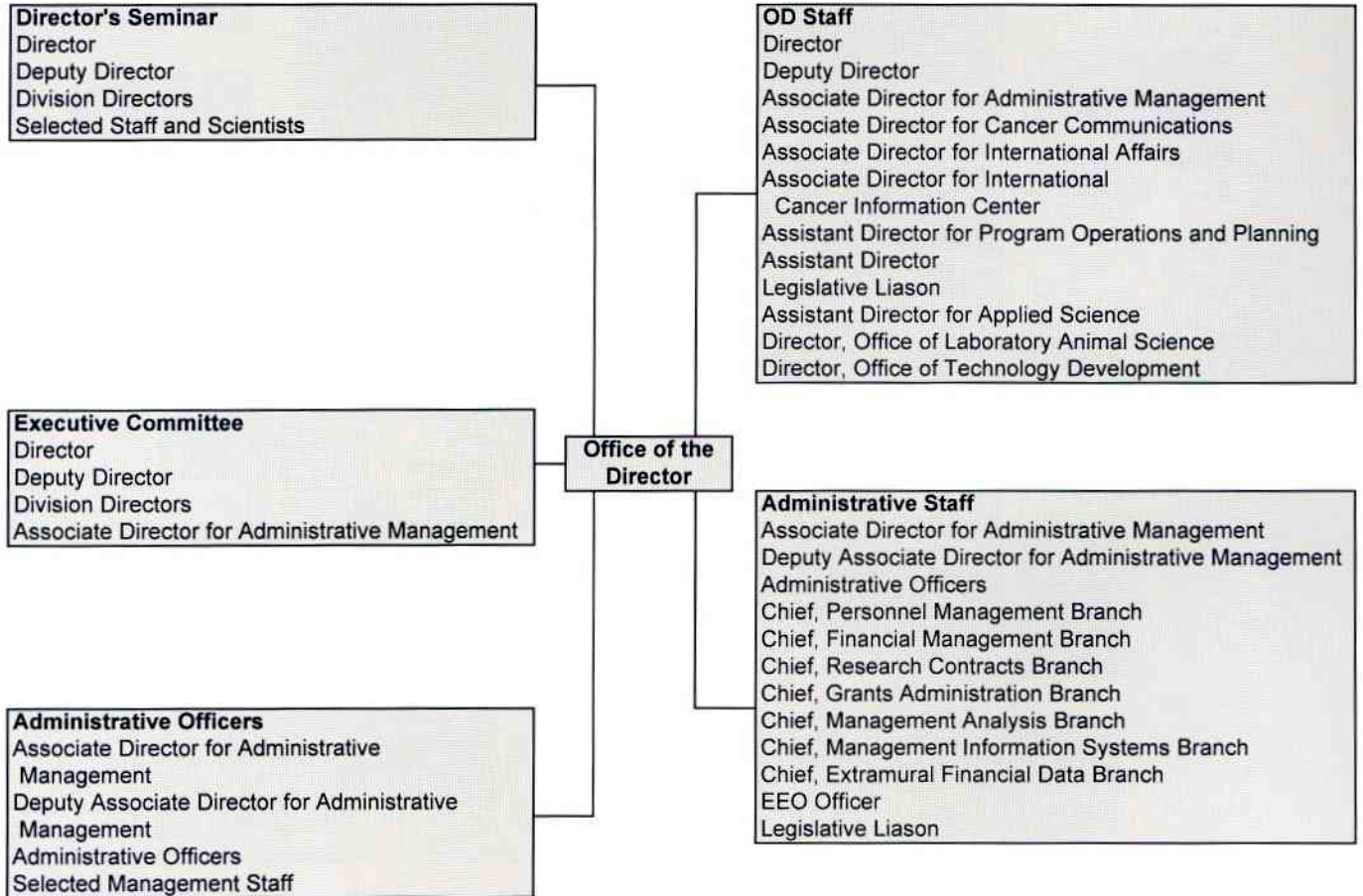
Division of Extramural Activities

Dr. Marvin Kalt, Director
Dr. Paulette S. Gray, Deputy Director (Acting)
Dr. Vincent Oliverio, Associate Director
Dr. Elliot Stonehill, Special Assistant to the Director

(1) Administers and directs the Institute's grant and contract review processing activities; (2) Provides initial technical and scientific merit review of grants and contracts for the Institute; (3) Represents the Institute on overall NIH extramural and collaborative program policy committees, coordinates such policy within NCI, and develops and recommends NCI policies and procedures as related to the review of grants and contracts; (4) Coordinates the Institute's review of research grant and training programs with the National Cancer Advisory Board; (5) Coordinates the implementation of committee management policies within the Institute and provides the Institute's staff support for the National Cancer Advisory Board; (6) Monitors and coordinates the operation of the divisional Boards of Scientific Counselors to assure uniformity and timeliness of the concept review of projects to be developed under contract or in response to RFAs; (7) Coordinates program planning and evaluation in the extramural area; (8) Provides scientific reports and analysis to the Institute's grant and central programs; and (9) administers programs to broaden participation by minorities in cancer-related research and training activities and to enhance the effectiveness of programs in cancer treatment and control in reaching the minority community and other historically underserved segments of the general population.



Information Flow for Program Implementation



Intramural Review Process

| | | | | | | |
|--|--|---|---|---|--|--|
| Board of Scientific Counselors | | | | | | |
| BSC Approves Site Visit Schedule | Chairman, BSC Selects Site Visit Chairman Site Visit Chairman Selects Site Visit Team | BSC Site Visit Team Reviews Material Prepared by Division | BSC Site Visit Team Inspects and Reviews Laboratory | Site Visit Team Prepares Report and Presents it to BSC. After Review and Approval, BSC Transmits Final Recommendations to the Division Director | | |
| Step 1 Scheduling and Approval | Step 2 Team Selection Site Visit | Step 3 Preparation for Site Visit | Step 4 Site Visit | Step 5 Site Visit Report and Recommendations | Step 6 Implementation of Recommendations | Step 7 Follow-up Report |
| NCI Divisions Division Prepares Proposed Site Visit Schedule | | Division Prepares Background Material on Laboratory to be Site Visited and Sends to Site Visit Team | Site Visit Preparation by Laboratory | | Division Implements Recommendations Contained in Site Visit Report | Division Prepares Report to BSC on Actions Taken |

Research Positions at the National Cancer Institute¹

The National Cancer Institute recognizes that one of the most valuable resources to be drawn upon in the fight against cancer is the wealth of scientific talent available in the U.S. and around the world. In an effort to attract and maintain the highest quality scientific staff, two personnel systems are used: the

U.S. Civil Service System and the PHS Commissioned Corps. In addition, the Staff Fellowship Program and the NIH Visiting Program have been designed to meet special needs. Other special programs are available for those who qualify.

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|--|--|---|--|
| I. Civil Service | | | |
| Civil Service (tenured) | Appropriate advanced education, experience and knowledge needed by NCI to conduct its programs. | Minimum starting Ph.D. - \$47,920 (GS-13/1) Physicians - \$59,099 (GS-13/8) | Office of Personnel Management; Contact Division Director of Laboratory Chief in area of interest or the NCI Personnel Office. |
| II. Special Appointment of Experts and Consultants | | | |
| Special Appointment of Experts and Consultants (non-tenured appointment which can be extended up to 4 years) | Applicants shall possess outstanding experience and ability as to justify recognition as authorities in their particular fields of activity. | Salary range is equivalent to GS-13/1 and with maximum limited to level IV of the Executive Schedule \$115,700 ² . | Final approval rests with the Division Director or Deputy Director, NCI depending on recommended action. |

¹Does not necessarily indicate that positions are currently available at the National Cancer Institute.

²Medical Officer (Research), GS-602 Special Rate Scale

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|--|--|--|---|
| III. Clinical Associate Program | | | |
| A. Clinical Associates | Initial appointment for 2 years with the possibility of 1-year extension. Graduate of accredited medical or osteopathic school and completion of internship. Completion of 2 or 3 years of clinical training beyond the M.D. degree. Must be a U.S. Citizen or a permanent U.S. resident. NOTE: Foreign M.D.'s in a U.S. residency training program are also eligible through a Fogarty International Center appointment. | \$38,500 1st yr \$40,500 2nd yr \$42,500 3rd yr | Apply to NIH Office of Education Building 10 Room 1C-129 |
| B. Pharmacology Research Associates (PRAT). Physicians committed to research careers in pharmacologic sciences, or clinical pharmacology. | Appointment for 2 years. Candidates must be U.S. citizens or permanent residents of the U.S. who have been awarded a doctoral degree or who have been certified by a university as meeting all the requirements leading to a doctorate. The degree must be in a biomedical or related science and must have been received within the 5 years preceding the date of application. | First year salaries range from \$33,500 for pH.Ds to \$37,000 for M.D.s based on years of postdoctoral experience. | Apply to PRAT Program, NIGMS Natcher Building Room 2AS-43 |

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|--|--|---|--|
| IV. Visiting Program (limited tenure)¹ | | | |
| A. Visiting Fellow (maximum 5 years) | 5 years or less of relevant postdoctoral experience or training. | First year salaries range from \$25,000 to \$42,000 based on years of postdoctoral experience | Contact Division Director or Laboratory Chief in area of interest. |
| B. Visiting Associate (1 year initial appointment with renewals to end of project) | 3+ years of postdoctoral experience or training with appropriate knowledge needed by NCI. | \$28,000 - (GS9/1) \$53,000 - (GS12/10) | Contact Division Director or Laboratory Chief in area of interest. |
| C. Visiting Scientist (duration of project) | 6+ years of postdoctoral experience with appropriate specific experience and knowledge needed. | \$41,000 - (GS12/1) \$87,000 - (GS15/10) | Contact Division Director or Laboratory Chief in area of interest. |

¹Under most circumstances, the various visiting programs are limited to non-citizens.

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|-----------------------------|---|--|--|
| V. Staff Fellowships | | | |
| A. Staff Fellowship | Physician or other doctoral degree equivalent who has less than 3 years of relevant professional level postdoctoral research experience. U.S. citizen or resident alien. Typical appointments are made for two years. Additional one-year extensions may also be made with a <u>maximum</u> of 7 years. | Physicians \$28,000 - \$48,196 (Maximum GS11/8) Other Doctors \$28,000 - \$47,013 (Maximum GS12/6) | Contact Division Director or Laboratory Chief in area of interest or the NCI Personnel Office. |
| B. Senior Staff Fellowship | Physician or other doctoral degree equivalent who has 3 to 7 years of relevant professional level postdoctoral research experience. U.S. citizen or resident alien. Typical appointments are made for two years. Additional one-year extensions may also be made with a <u>maximum</u> of 7 years. | Physicians \$39,000 - \$73,472 (Maximum GS13/10) Other Doctors \$33,504 - \$62,293 (Maximum GS13/10) | Contact Division Director or Laboratory Chief in area of interest or the NCI Personnel Office. |

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|---|--|-----------------------|--|
| VI. Civil Service Summer Employment Programs | | | |
| Summer Aides | Provides summer employment opportunity for students who meet economic needs criteria. Must be 16 years of age or older. Disabled students are not required to meet economic criteria. Noncitizens may compete provided they have permanent visa status and are from a country allied with the United States. | Federal minimum wage. | Register with the local office of the State Employment service and apply to NCI. |

VII. Special Programs

| | | | |
|--|---|---|---|
| A. Guest Researcher-organization other than NIH, PHS | Usually a scientist, engineer or other scientifically trained specialist who would benefit from the use of NCI facilities in furthering his or her research. Cannot perform services for NCI. | Established by sponsoring organization. | Contact Division Director or Laboratory Chief in area of interest; also apply to sponsoring agency, e.g., American Cancer Society, Eleanor Roosevelt Cancer Foundation, Leukemia Society of America, Inc., etc. |
|--|---|---|---|

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|--|--|---|---|
| <p>B. Commissioned Officer Student Training and Extern Program (COSTEP) Program (operates year-round). Maximum 120 days per 12-month period.</p> | <p>U.S. citizen. Must have completed one year of study in a medical, dental, podiatry, optometry or veterinary school or a minimum of two years of baccalaureate program in a health related field such as engineering, nursing, pharmacy, etc. May be enrolled in a master's or doctoral program in a health related field (designated by the Assistant Secretary for Health). Physical requirements of PHS Commissioned Corps. Plans to return to college.</p> | <p>Receive the basic pay quarters (if appropriate), and subsistence allowance of a Junior Assistant Health Service Officer (pay grade 0-1).</p> | <p>Apply to Director, Division of Commissioned Personnel Attention: COSTEP Coordinator Room 4-35, Parklawn Building, 5600 Fishers Lane, Rockville, MD. 20857.</p> |
| <p>C. Fogarty International Scholars in Residence Program.</p> | <p>International reputation, productivity, demonstrated ability in biomedical field.</p> | <p>\$90,000 for 1 year.</p> | <p>Nominations are submitted to Fogarty Center by Institute Director, any senior tenured member of the NIH scientific staff, or former scholar.</p> |
| <p>D. Stay-in-School Program</p> | <p>Provides employment opportunity for students who meet economic needs criteria, attend accredited schools on a full-time basis, and are in good academic standing. Must be 16 years of age or older. Disabled students are not required to meet economic criteria. Noncitizens may compete provided they are from a country allied with the United States.</p> | <p>Salary is commensurate with duties assigned and student's education and/or experience.</p> | <p>Register with the local office of the State Employment Service and apply to NCI Personal Office, EPS, Room 537, 6120 Executive Blvd., Rockville, MD 20892-7209. No deadline required for applying. However, no new appointments are made between May 1 to August 30.</p> |

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|--|--|--------------------|--|
| E. The Federal Junior Fellowship Program | Graduating high school senior in a public or private school. Must have demonstrated satisfactory academic performance with accumulative G.P.A. equivalent to a "C+" or above. Must plan to attend or have been accepted for admission to an accredited college or university. Must qualify under financial needs criteria based upon family income. Must be a U.S. citizen or a resident of American Samoa or Swains island. May be a non-citizen if lawfully admitted to the U.S. as a permanent resident and will be able to meet citizenship requirements prior to conversion and is a national of an allied country. | GS-2 through GS-5. | Nominations are submitted directly to NIH by high school principals or counselors. |
| F. Special Volunteer Program | Volunteer service may be accepted for direct patient care, clerical assignments, technical assistance, or any other activities necessary to carry out the authorized functions of the NCI. Applicants must be at least 16 years of age (work permit required if under 18). | N/A | Contact Division Director or Laboratory Chief in area of interest. |

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|----------------------------------|---|----------------------|---|
| G. Cooperative Education Program | Must be 16 years of age or older, enrolled in an accredited educational program, high school, undergraduate, graduate, or professional degree program and be in good academic standing (GPA at least 2.0). School must participate in the coop program. Must be enrolled in a field of study related to the assigned work with at least half-time academic course load. U.S. citizen or national (resident of American Samoa or Swains Island) or noncitizen lawfully admitted to the U.S. as a permanent resident who will be able to meet citizenship requirements prior to conversion, and is a national of a country allied with the U.S. | GS-1 through GS-11 | Contact NCI Personal Office, EPS, Room 537, 6120 Executive Blvd., Rockville, MD 20892-7209. |

VIII. Other Training Programs

| | | | |
|---|--|--|--|
| A. Cancer Prevention Fellowship Program | Must be an M.D., D.D.S., D.O., O.R., Ph.D., or other doctoral degree in a related discipline (epidemiology, biostatistics, and the biomedical, nutritional, public health, or behavioral sciences). Must be a U.S. citizen or resident alien eligible for citizenship within four years. | First year for an M.D., D.D.S., or D.O. \$30,000 - \$41,000 for Ph.D. \$22,000 - \$35,000. | Apply to Program Director, CFPF, Executive Plaza South, Room T41, MSC 7105, 6120 Executive Blvd., Rockville, MD 20892-7209. Bethesda, Maryland, 20892. |
|---|--|--|--|

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|-----------------------------------|--|--|---|
| B. Biotechnology Training Program | <p>Physicians with little or no experience or training in fundamental research, but with an interest in biotechnology including its application to prevention and new treatment and diagnostic techniques, would be eligible. Ph.D. scientists with little or no experience or training in clinically related programs but with an interest in clinical applications of fundamental research methodology related to biotechnology would also be eligible. Typically, these candidates will have less than three years postdoctoral experience. The Biotechnology Training Program is established for United States citizens, or resident aliens who will be eligible for U.S. citizenship within four years.</p> | <p>First year Ph.D. \$25,000 - \$38,000 Physicians \$37,000 - \$45,000</p> | <p>Contact Division Director or Laboratory Chief in area of interest.</p> |
| C. Cancer Nurse Training Program | <p>Applications will be accepted from Graduates of NLN accredited baccalaureate nursing programs. Each candidate must submit academic transcripts demonstrating a minimum of a "B" average in undergraduate work, three references regarding their academic work and clinical capability, a letter describing their interest in the program, and a Personal Qualification Statement, SF-171.</p> | <p>Stipends for the program will be \$2,600 per month.</p> | <p>Contact the Division of Cancer Treatment.</p> |

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|--------------------------------------|--|---|--|
| D. Student Research Training Program | <p>The review and selection of candidates, as well as the day-to-day administration of the fellowships, will be the responsibility of each Division's Administrative Office. Applicants must be bona fide high school, college, graduate or medical school students be 16 years of age, have a cumulative GPA of 2.75 or above, be either a U.S. citizen or resident alien. The length of the training fellowships may vary from 2 to 6 months, not to exceed 6 months during one 12-month period.</p> | <p>Stipends are based on education and experience at a pay range of \$802 - \$1,872 per month.</p> | <p>Contact Division Director or Laboratory Chief in area of interest. Application deadlines are March 1 for spring/summer months and October 1 for fall/winter months.</p> |
| E. General Fellowship Program | <p>M.D., Ph.D. or equivalent degrees as well as pre-doctoral candidates pursuing graduate work with the aim of achieving a doctoral degree. U.S. citizens, permanent residents, or foreign citizens are eligible.</p> | <p>Salary is commensurate with the duties assigned and candidate's education and/or experience.</p> | <p>Contact Division Director or Laboratory Chief in area of interest.</p> |

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|---|--|---|---|
| F. Cancer Epidemiology and Biostatistics Training Program | M.D.s and Ph.D.s with an interest in and an aptitude for epidemiology and/or biostatistical research in cancer. Ph.D. candidates in approved doctoral programs in epidemiology or biostatistics whose research would be the source of their dissertation. Master's level scientists whose degree is in a discipline related to epidemiology or biostatistics. Must be U.S. citizen or resident alien who will be eligible for U.S. citizenship within four years. | First year for M.D. and Ph.D. Mathematical Statisticians \$31,000 - \$42,000 for other Ph.D. \$23,000-\$36,000 for Master's level \$16,000 - \$20,000 | Contact the Administrative Office of the Division of Cancer Etiology. |
| G. Intramural Research Training Award (IRTA) | <p>(1) Postdoctoral: Appointments of 1 or 2 years with a maximum of 5 years to candidates with physician or other doctoral degree in the biomedical, behavioral or related sciences and 7 or fewer years of relevant postdoctoral research experience.</p> <p>(2) Predoctoral: Fellowships are granted to students enrolled in PhD, MD, DDS, DMD, DVM, or equivalent degree programs. Students will have completed their graduate course work and will engage full-time in a laboratory research program for the purpose of developing and writing a thesis in an intramural laboratory.</p> | <p>First year salaries range from \$25,000 - \$38,000 based on years of experience.</p> <p>Based on years of post-baccalaureate education ranging from \$16,000 - \$21,000.</p> | <p>Contact Division Director or Laboratory Chief in area of interest.</p> <p>Contact Division Director or Laboratory Chief in area of interest.</p> |

| Position | Eligibility | Annual Salary | Mechanism of Entry |
|---|---|--|---|
| H. Technology Transfer Fellowship Program | Physicians, PhDs, JDs(lawyers), individuals with a master's degree in health communications, biomedical science, behavioral science, computer science, informatics, library science, health education, marketing, journalism, English, a graduate degree in law, or a graduate degree in another discipline with legal/paralegal expertise, with little or no experience or training in technology transfer or communications research but with an interest in these areas. | Based on years of (1) postdoctoral experience starting at \$25,000 - \$38,000 or (2) post-Master's degree starting at \$22,000 - \$34,000. | Contact following program in area of interest: International Cancer Information Center, the Office of Cancer Communications, the Division of Cancer Prevention and Control, the Office of Technology Development, or the Planning, Evaluation, and Analysis Branch. |

Number of Deaths for the Five Leading Cancer Sites by Age Group and Sex

| All Ages | | Under 15 | | 15-34 | | 35-54 | | 55-74 | | 75+ | |
|----------------|----------------|------------------------|-------------|------------------------|------------------------|------------------------|----------------|----------------|----------------|----------------|----------------|
| Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| Lung | Lung | Leukemia | Leukemia | Leukemia | Breast | Lung | Breast | Lung | Lung | Lung | Lung |
| 91,600 | 52,020 | 350 | 260 | 661 | 660 | 8,726 | 9,188 | 55,836 | 30,126 | 26,881 | 16,387 |
| Prostate | Breast | Brain & CNS | Brain & CNS | Non-Hodgkin's Lymphoma | Leukemia | Colon & Rectum | Lung | Colon & Rectum | Breast | Prostate | Colon & Rectum |
| 33,563 | 43,582 | 252 | 220 | 497 | 433 | 2,342 | 5,367 | 13,823 | 19,900 | 20,909 | 15,634 |
| Colon & Rectum | Colon & Rectum | Endocrine | Endocrine | Brain & CNS | Brain & CNS | Non-Hodgkin's Lymphoma | Colon & Rectum | Prostate | Colon & Rectum | Colon & Rectum | Breast |
| 28,025 | 28,751 | 112 | 70 | 414 | 328 | 1,716 | 1,959 | 12,306 | 10,988 | 11,657 | 13,834 |
| Pancreas | Pancreas | Non-Hodgkin's Lymphoma | Soft Tissue | Melanoma | Cervix | Brain & CNS | Ovary | Pancreas | Ovary | Pancreas | Pancreas |
| 12,373 | 13,161 | 63 | 33 | 240 | 307 | 1,577 | 1,750 | 6,730 | 6,605 | 4,299 | 6,637 |
| Leukemia | Ovary | Soft Tissue | Bone | Hodgkin's | Non-Hodgkin's Lymphoma | Pancreas | Cervix | Esophagus | Pancreas | Leukemia | Ovary |
| 10,286 | 13,028 | 48 | 28 | 233 | 209 | 1,298 | 1,533 | 4,600 | 5,669 | 3,734 | 4,527 |

Source: Mortality tape (1991) from National Center for Health Statistics.

Relationship of Cancer to the Leading Causes of Death in the United States

| Rank | Cause | Number of Deaths | Crude Death Rate per 100,000 Population | Percent of Total Deaths |
|------|--|------------------|---|-------------------------|
| | All Causes | 2,168,492 | 860.2 | 100.0% |
| 1 | Diseases of the Heart | 720,755 | 285.9 | 33.2 |
| 2 | CANCER | 514,636 | 204.1 | 23.7 |
| 3 | Cerebrovascular | 143,467 | 56.9 | 6.6 |
| 4 | Bronchitis, Emphysema & Asthma | 90,640 | 35.9 | 4.2 |
| 5 | Accidents | 89,227 | 35.4 | 4.1 |
| 6 | Pneumonia & Influenza | 77,846 | 30.9 | 3.6 |
| 7 | Diabetes Mellitus | 48,949 | 19.4 | 2.3 |
| 8 | Suicide | 30,790 | 12.2 | 1.4 |
| 9 | Human Immunodeficiency Virus Infection | 29,545 | 11.7 | 1.4 |
| 10 | Homicide | 26,432 | 10.5 | 1.2 |
| 11 | Cirrhosis of the Liver | 25,411 | 10.1 | 1.2 |
| 12 | Nephritis & Nephrosis | 21,358 | 8.5 | 1.0 |
| 13 | Septicemia | 19,688 | 7.8 | 0.9 |
| 14 | Atherosclerosis | 17,419 | 6.9 | 0.8 |
| 15 | Diseases of Infancy | 16,781 | 6.7 | 0.8 |
| | Other & Ill-defined | 295,998 | 117.4 | 13.6 |

Source: Mortality Tape (1991) from National Center for Health Statistics.

**Estimated New Cancer
Cases and Deaths
by Sex for All Sites
1994**

| | Estimated New Cases | | | Estimated Deaths | | |
|---------------------------------|---------------------|---------|---------|------------------|---------|---------|
| | Total | Male | Female | Total | Male | Female |
| All Sites | 1,208,000 | 632,000 | 576,000 | 538,000 | 283,000 | 255,000 |
| Oral Cavity & Pharynx | 29,600 | 19,800 | 9,800 | 7,925 | 5,150 | 2,775 |
| Lip | 3,300 | 2,800 | 500 | 75 | 50 | 25 |
| Tongue | 6,000 | 3,800 | 2,200 | 1,750 | 1,100 | 650 |
| Mouth | 11,100 | 6,600 | 4,500 | 2,100 | 1,200 | 900 |
| Pharynx | 9,200 | 6,600 | 2,600 | 4,000 | 2,800 | 1,200 |
| Digestive System | 233,300 | 123,100 | 110,200 | 121,450 | 64,550 | 56,900 |
| Esophagus | 11,000 | 8,000 | 3,000 | 10,400 | 7,800 | 2,600 |
| Stomach | 24,000 | 15,000 | 9,000 | 14,000 | 8,400 | 5,600 |
| Small Intestine | 3,600 | 2,000 | 1,600 | 950 | 500 | 450 |
| Colon | 107,000 | 52,000 | 55,000 | 49,000 | 24,000 | 25,000 |
| Rectum | 42,000 | 23,000 | 19,000 | 7,000 | 3,800 | 3,200 |
| Liver & Intrahepatic Bile Duct | 16,100 | 8,800 | 7,300 | 13,200 | 7,200 | 6,000 |
| Pancreas | 27,000 | 13,000 | 14,000 | 25,900 | 12,400 | 13,500 |
| Other & Digestive | 2,600 | 1,300 | 1,300 | 1,000 | 450 | 550 |
| Respiratory System | 189,000 | 112,800 | 76,200 | 158,200 | 97,900 | 60,300 |
| Larynx | 12,500 | 9,800 | 2,700 | 3,800 | 3,000 | 800 |
| Lung & Bronchus | 172,000 | 100,000 | 72,000 | 153,000 | 94,000 | 59,000 |
| Other & Unspecified Respiratory | 4,500 | 3,000 | 1,500 | 1,400 | 900 | 500 |
| Bones & Joints | 2,000 | 1,100 | 900 | 1,075 | 600 | 475 |
| Soft Tissues | 6,000 | 3,300 | 2,700 | 3,300 | 1,600 | 1,700 |
| Melanomas of Skin | 32,000 | 17,000 | 15,000 | 6,900 | 4,300 | 2,600 |
| Breast | 183,000 | 1,000 | 182,000 | 46,300 | 300 | 46,000 |
| Genital Organs | 283,400 | 208,100 | 75,300 | 63,725 | 38,525 | 25,200 |
| Cervix Uteri | 15,000 | | 15,000 | 4,600 | | 4,600 |
| Corpus and Uterus, NOS | 31,000 | | 31,000 | 5,900 | | 5,900 |
| Ovary | 24,000 | | 24,000 | 13,600 | | 13,600 |
| Other Female Genital | 5,300 | | 5,300 | 1,100 | | 1,100 |
| Prostate | 200,000 | 200,000 | | 38,000 | 38,000 | |
| Testis | 6,800 | 6,800 | | 325 | 325 | |
| Other Male Genital | 1,300 | 1,300 | | 200 | 200 | |
| Urinary System | 78,800 | 55,000 | 23,800 | 21,900 | 13,800 | 8,100 |
| Bladder | 51,200 | 38,000 | 13,200 | 10,600 | 7,000 | 3,600 |
| Kidney & Other Urinary | 27,600 | 17,000 | 10,600 | 11,300 | 6,800 | 4,500 |
| Eye and Orbit | 1,750 | 950 | 800 | 250 | 125 | 125 |
| Brain & Central Nervous System | 17,500 | 9,600 | 7,900 | 12,600 | 6,800 | 5,800 |
| Endocrine Glands | 14,450 | 4,150 | 10,300 | 1,725 | 750 | 975 |
| Thyroid | 13,000 | 3,400 | 9,600 | 1,025 | 400 | 625 |
| Other Endocrine | 1,450 | 750 | 700 | 700 | 350 | 350 |
| Leukemias | 28,600 | 16,200 | 12,400 | 19,100 | 10,500 | 8,600 |
| Lymphomas and Myelomas | 65,600 | 35,900 | 29,700 | 32,550 | 17,100 | 15,450 |
| Hodgkin's Disease | 7,900 | 4,400 | 3,500 | 1,550 | 900 | 650 |
| Non-Hodgkin's Lymphomas | 45,000 | 25,000 | 20,000 | 21,200 | 11,200 | 10,000 |
| Multiple Myeloma | 12,700 | 6,500 | 6,200 | 9,800 | 5,000 | 4,800 |
| All Other and Unspecified Sites | 43,000 | 24,000 | 19,000 | 41,000 | 21,000 | 20,000 |

SOURCE: Boring CC, Squires T, Tong T, Montgomery S., *Cancer Statistics 1994*.
CA Cancer J Clin 1994; 44:7-26. Excludes basal and squamous cell skin and in
situ carcinomas except urinary bladder. Incidence estimates are based on
rate from the NCI SEER Program 1988-90.

The Cost of Cancer

The direct cost of cancer is derived from the figures for care of patients. It does not include the cost of the productivity lost while individuals are away from their work due to treatment of disability or the value of lost productivity due to premature death. Figures for the direct cost of cancer and for all health care for 1990 are as follow:

| (in Millions) | |
|---|--------------------|
| <u>All Costs</u> | <u>Direct Cost</u> |
| All Cancers | \$ 35,256 |
| All Health Care | \$585,300 |
| Percent Relationship of Cancer to Total | 6% |

Sources:

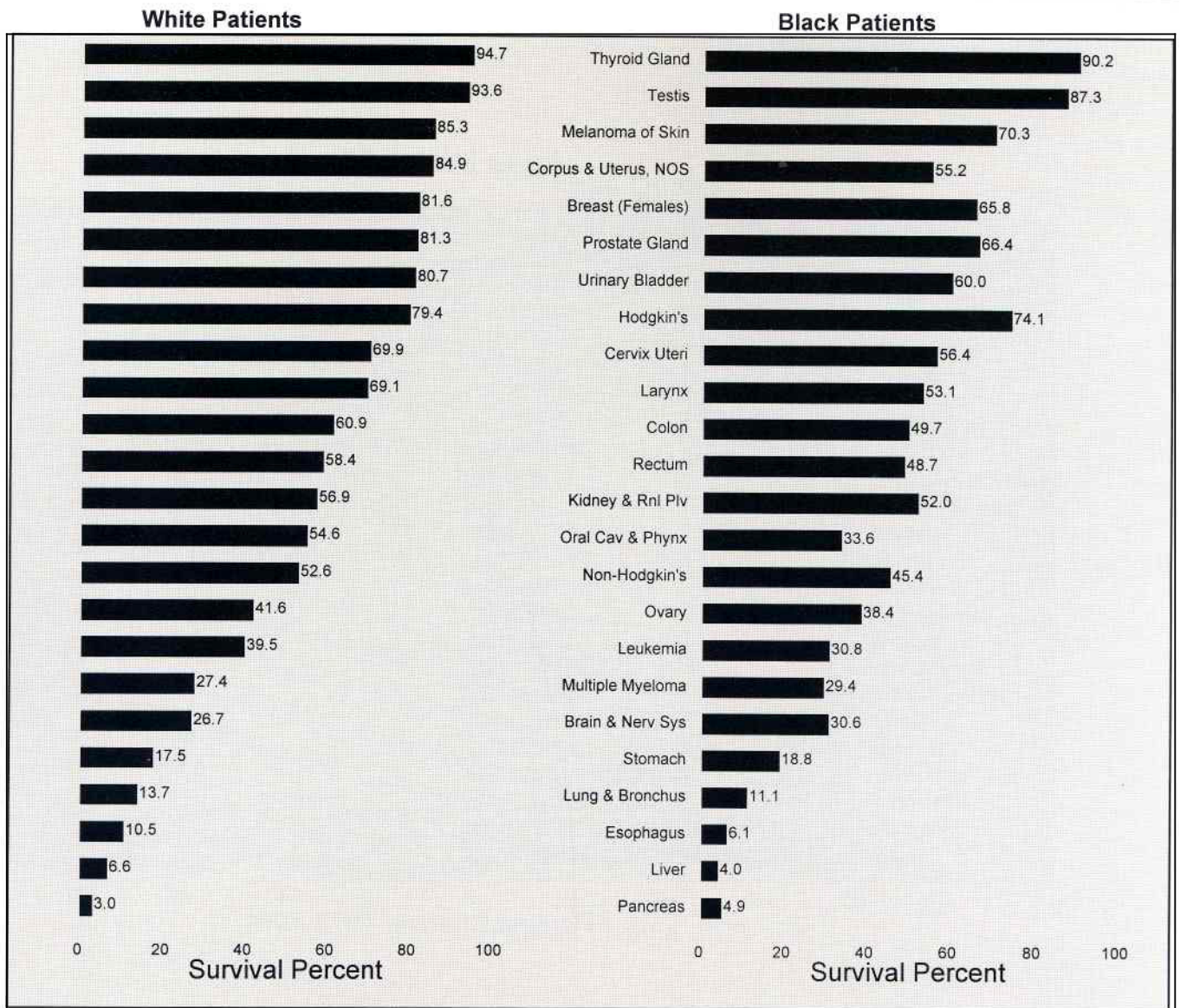
Brown, M.L. The National Economic Burden of Cancer: An Update. *Journal of the National Cancer Institute*, 1990, 82:1881-1814.

Office of the Actuary, Health Care Financing Administration.

**Average Years of Life Lost
Per Person Dying of Cancer
All Races, Both Sexes, 1991**

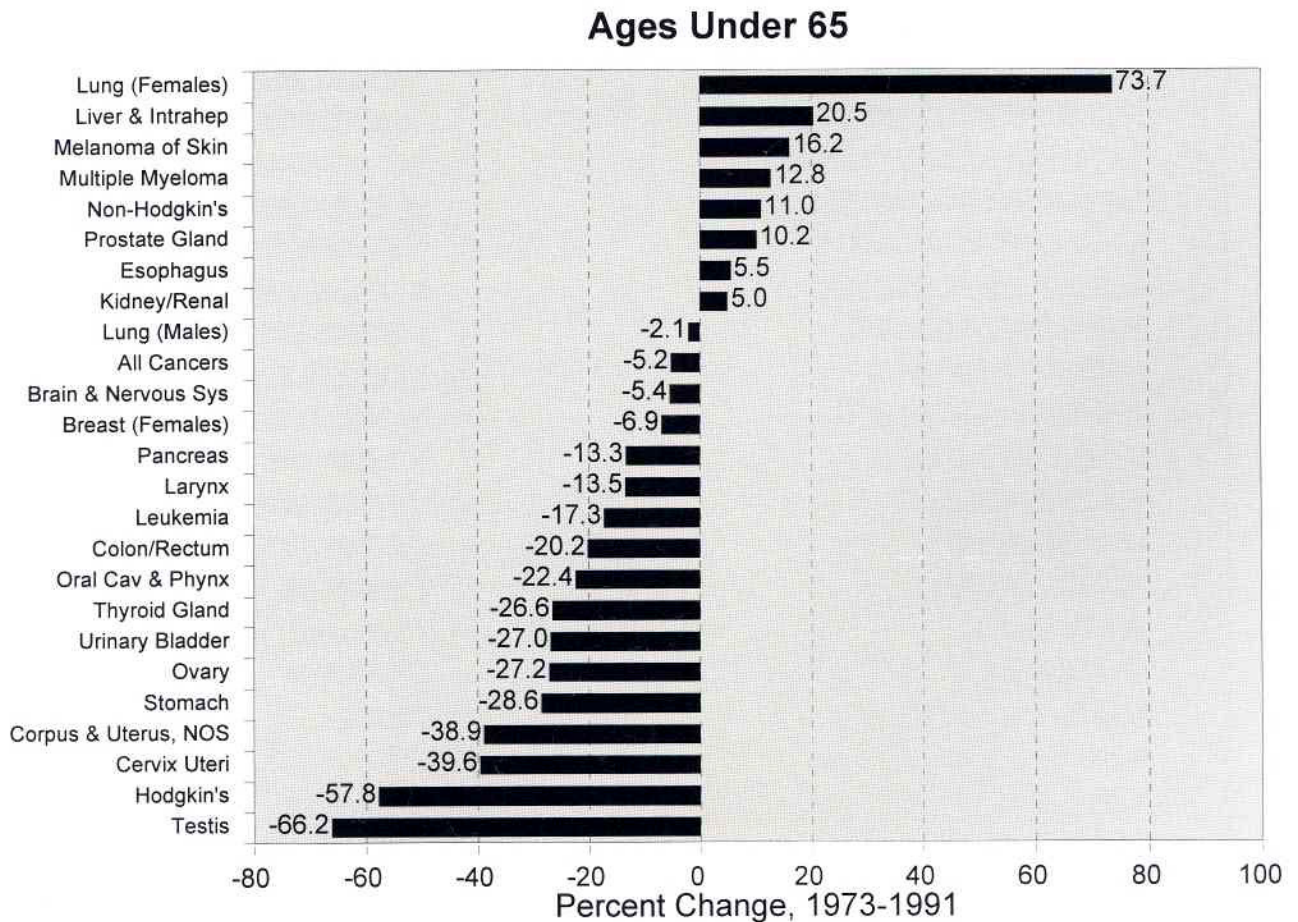


**5 Year Relative
Survival Rates, by Site
White and Black Patients
1983 to 1990**



Data From SEER Program
1984-1990
Males and Females

**Cancer Mortality Rates
Changes from 1973 to 1991
(Ages Under 65)**

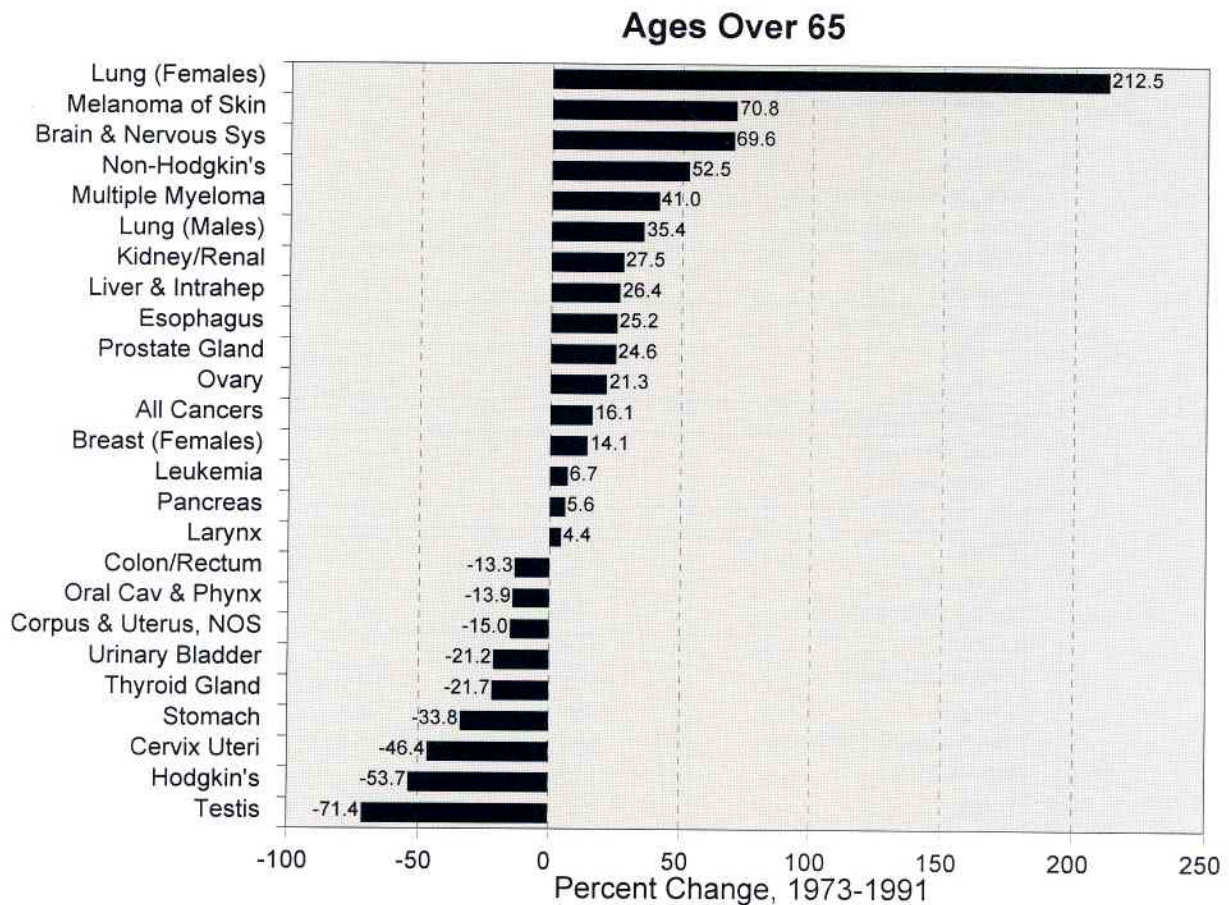


Note:

Progress and problems:

This graph illustrates percent changes in the annual death rate for a wide range of cancers. Cancers to the right of the zero axis have had increased cancer mortality rates, those to the left have had decreased mortality rates. If the graph is turned counter-clockwise, on its side, the bars pointing down show the major tumors in which a significant reduction in annual death rate has occurred. Progress is apparent: a reduction has occurred in the annual death rates since 1973 in both common and uncommon cancers. This definitely shows progress in the age group under 65, albeit more progress needs to be made.

Cancer Mortality Rates
Changes from 1973 to 1991
(Ages Over 65)



Note:

Progress and problems:

Comparing this chart to that for individuals under 65, it is clear that not as much progress is being made in reducing cancer death rates in older groups. The cancer deaths to the right of the zero axis have risen, those to the left have decreased. This graph should be compared to the accompanying graph addressing changes in mortality rates for people under age 65. Issues such as low-income, patterns of medical care, and other related factors are thought to be important considerations in the older population.

Cancer Mortality Rates
United States, 1987-1991

| Cancer Site | Mortality Rate per 100,000 | | Ratio Blacks/Whites |
|----------------------------------|----------------------------|--------|------------------------|
| | Blacks | Whites | |
| All Sites | 226.2 | 169.0 | 1.3 |
| Males | 316.8 | 213.3 | 1.5 |
| Females | 166.9 | 139.6 | 1.2 |
| Esophagus | 8.5 | 3.0 | 2.8 |
| Cervix Uteri | 6.7 | 2.6 | 2.6 |
| Prostate | 52.0 | 23.6 | 2.2 |
| Multiple Myeloma | 5.8 | 2.7 | 2.1 |
| Larynx | 2.8 | 1.2 | 2.3 |
| Stomach | 8.9 | 4.3 | 2.1 |
| Oral Cavity and Pharynx | 5.2 | 2.7 | 1.9 |
| Corpus & Uterus NOS | 6.0 | 3.2 | 1.9 |
| Liver & Intrahep. | 4.2 | 2.5 | 1.7 |
| Pancreas | 11.9 | 8.1 | 1.5 |
| Lung and Bronchus | 61.2 | 48.6 | 1.3 |
| Males | 105.5 | 73.0 | 1.4 |
| Females | 30.4 | 30.9 | 1.0 |
| Colon and Rectum | 23.5 | 18.8 | 1.3 |
| Breast (Females) | 31.2 | 27.2 | 1.1 |
| <50 years | 9.2 | 5.9 | 1.6 |
| > 50 years | 99.1 | 93.1 | 1.1 |
| Thyroid | 0.4 | 0.3 | 1.3 |
| Urinary Bladder | 3.3 | 3.3 | 1.0 |
| Kidney & Renal Pelvis | 3.3 | 3.5 | 0.9 |
| Leukemia | 6.0 | 6.4 | 0.9 |
| Hodgkin's Disease | 0.6 | 0.6 | 1.0 |
| Ovary | 6.5 | 8.0 | 0.8 |
| Non-Hodgkin's Lymphomas | 4.3 | 6.4 | 0.7 |
| Brain & CNS | 2.6 | 4.5 | 0.6 |
| Testis | 0.1 | 0.3 | 0.3 |
| Melanoma of Skin | 0.4 | 2.5 | 0.2 |
| All Sites Except Lung & Bronchus | 165.0 | 120.4 | 1.4 |
| Males | 211.3 | 140.3 | 1.5 |
| Females | 136.5 | 108.8 | 1.3 |

NOTE: The annual number of cancer deaths per 100,000 persons is derived from estimates of the National Center for Health Statistics, adjusted to the 1970 US population age distribution.

Cancer Incidence Rates
Unites States, 1987-1991

| Cancer Site | Incidence Rates per 100,000 | | Ratio |
|----------------------------------|-----------------------------|--------|---------------|
| | Blacks | Whites | Blacks/Whites |
| All Sites | 422.1 | 392.0 | 1.1 |
| Males | 557.2 | 464.0 | 1.2 |
| Females | 331.8 | 348.0 | 1.0 |
| Esophagus | 10.0 | 3.4 | 2.9 |
| Multiple Myeloma | 9.1 | 4.1 | 2.2 |
| Cervix | 14.0 | 7.8 | 1.8 |
| Stomach | 12.7 | 6.7 | 1.9 |
| Liver & Intrahep. | 4.7 | 2.4 | 2.0 |
| Pancreas | 13.8 | 8.6 | 1.6 |
| Larynx | 7.1 | 4.4 | 1.6 |
| Prostate | 163.1 | 121.2 | 1.3 |
| Lung and Bronchus | 77.2 | 57.9 | 1.3 |
| Males | 122.4 | 80.7 | 1.5 |
| Females | 44.5 | 41.3 | 1.1 |
| Oral Cavity and Pharynx | 14.0 | 10.5 | 1.3 |
| Kidney and Renal Pelvis | 9.5 | 8.8 | 1.1 |
| Colon and Rectum | 52.4 | 47.8 | 1.1 |
| Colon | 40.6 | 34.0 | 1.2 |
| Rectum | 11.9 | 13.8 | 0.9 |
| Leukemia | 8.9 | 10.2 | 0.9 |
| Breast (Females) | 94.0 | 113.2 | 0.8 |
| <50 years | 33.0 | 33.2 | 1.0 |
| >50 years | 281.9 | 359.8 | 0.8 |
| Ovary | 10.3 | 15.6 | 0.7 |
| Non-Hodgkin's Lymphomas | 10.2 | 15.0 | 0.7 |
| Brain and Other Nervous | 3.9 | 6.7 | 0.6 |
| Corpus & Uterus NOS | 14.5 | 22.2 | 0.7 |
| Hodgkin's Disease | 2.1 | 3.1 | 0.7 |
| Thyroid | 2.5 | 4.5 | 0.6 |
| Bladder | 9.7 | 18.2 | 0.5 |
| Testis | 0.8 | 5.1 | 0.2 |
| Melanoma of Skin | 0.9 | 12.4 | 0.1 |
| All Sites Except Lung & Bronchus | 344.9 | 334.0 | 1.0 |
| Males | 434.8 | 383.3 | 1.1 |
| Females | 287.2 | 306.7 | 0.9 |

NOTE: The annual number of new cancer cases per 100,000 persons is derived from NCI's SEER Program, adjusted to the 1970 US population age distribution.

**The Prevalence of Cancer:
Estimated Number of Persons
Diagnosed With Cancer
United States, 1994**

| | 1994 Estimated Prevalence | | |
|--------------------------|---------------------------|-----------|-----------|
| | Total | Males | Females |
| ALL SITES | 7,184,000 | 2,808,500 | 4,375,500 |
| Oral & Pharynx | 194,100 | 120,300 | 73,800 |
| Stomach | 68,600 | 39,400 | 29,200 |
| Colon/Rectal | 1,227,800 | 577,300 | 650,500 |
| Colon | 885,600 | 403,300 | 482,300 |
| Rectum | 342,200 | 174,000 | 168,200 |
| Pancreas | 24,200 | 10,400 | 13,800 |
| Larynx | 135,600 | 108,600 | 27,000 |
| Lung & Bronchus | 380,900 | 211,800 | 169,100 |
| Melanoma of Skin | 389,800 | 184,700 | 205,100 |
| Breast | 1,721,700 | - | 1,721,700 |
| Cervix Uteri | 183,900 | - | 183,900 |
| Corpus & Uterus | 486,000 | - | 486,000 |
| Ovary | 170,500 | - | 170,500 |
| Prostate Gland | 565,600 | 565,600 | - |
| Testis | 109,400 | 109,400 | - |
| Urinary Bladder | 541,200 | 385,000 | 156,200 |
| Kidney & Renal Pelvis | 158,700 | 97,700 | 61,000 |
| Brain and Nervous System | 81,600 | 42,100 | 39,500 |
| Thyroid | 181,300 | 43,900 | 137,400 |
| Hodgkin's Disease | 136,300 | 72,800 | 63,500 |
| Non-Hodgkin's Lymphomas | 260,300 | 129,300 | 131,000 |
| Leukemia | 125,000 | 65,200 | 59,800 |

NOTE: Previous published prevalence national estimates of cancer have been revised using age-specific cancer rates. There has been no decline in prevalence-the number of cancer survivors has increased during recent years.

**Fiscal Year
1994 Budget**

(Dollars in Thousands)

A. Actual Obligations Resulting From Appropriated Funds:

| | |
|--|------------------|
| FY 1994 Appropriation | \$2,082,267 |
| Rescission in accordance with P.L. 103-211 | -5,885 |
| Lapse | -164 |
| Actual Subtotal | 2,076,218 |

| | |
|---|------------------|
| Comparative transfer to the Office of AIDS Research, NIH for HIV Activities | -212,868 |
| Actual NCI Obligations | 1,863,350 |

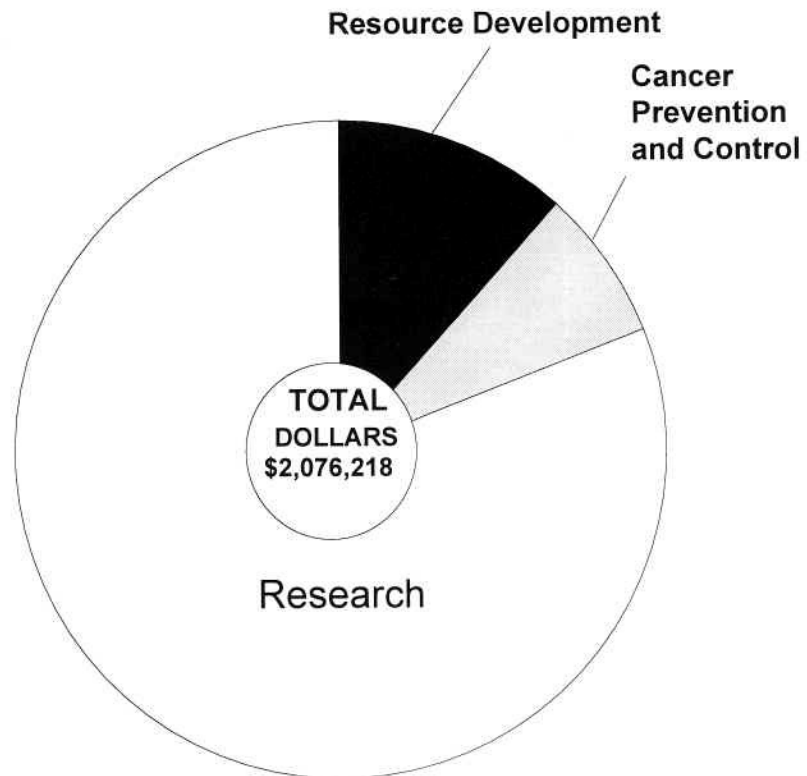
B. Reimbursable Obligations:

| | |
|---|---------------|
| AIDS Reimbursement from Office of the Director, NIH | 1,973 |
| Other Reimbursements | 8,883 |
| Reimbursements | 10,856 |

C. Total NCI Obligations **\$1,874,206**

Program Structure
Fiscal Year 1994

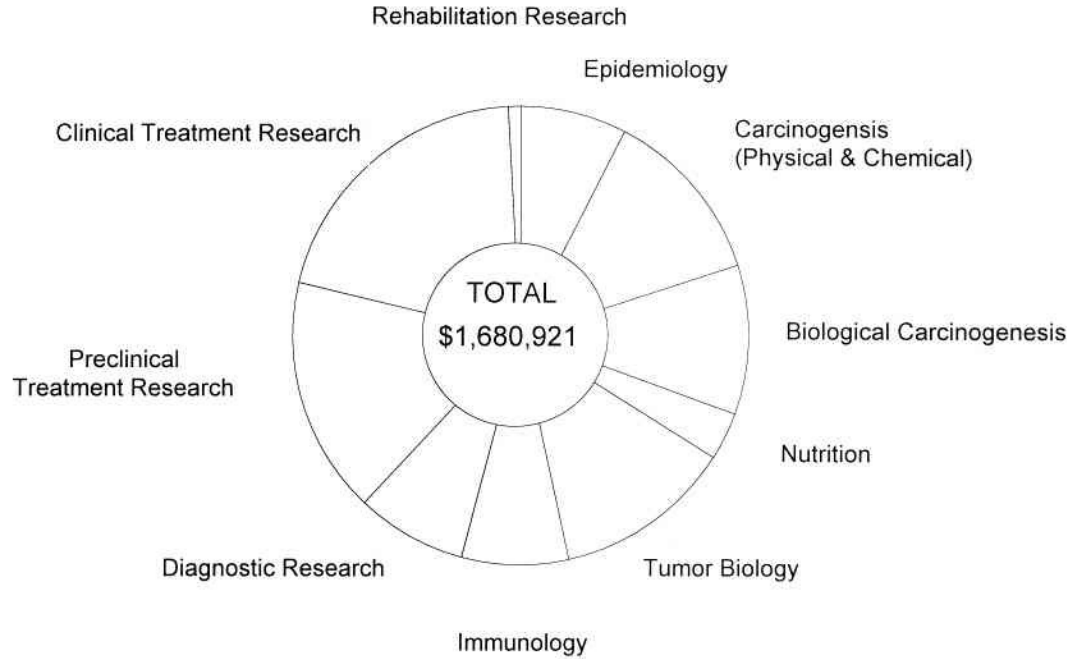
(Dollars in Thousands)



| Budget Activity | Dollars | Percent |
|--------------------------------------|--------------------|---------------|
| Research | | |
| Cancer Causation | \$584,895 | 28.2% |
| Detection and Diagnosis Research | 143,059 | 6.9% |
| Treatment Research | 641,773 | 30.9% |
| Cancer Biology | 311,194 | 15.0% |
| Subtotal Research | 1,680,921 | 81.0% |
| Resource Development | | |
| Cancer Centers Support | 160,534 | 7.7% |
| Research Manpower Development | 64,086 | 3.1% |
| Construction | 16,822 | 0.8% |
| Subtotal Resource Development | 241,442 | 11.6% |
| Cancer Prevention and Control | 153,855 | 7.4% |
| Total NCI | \$2,076,218 | 100.0% |

NCI Research Programs
Fiscal Year 1994

(Dollars in Thousands)

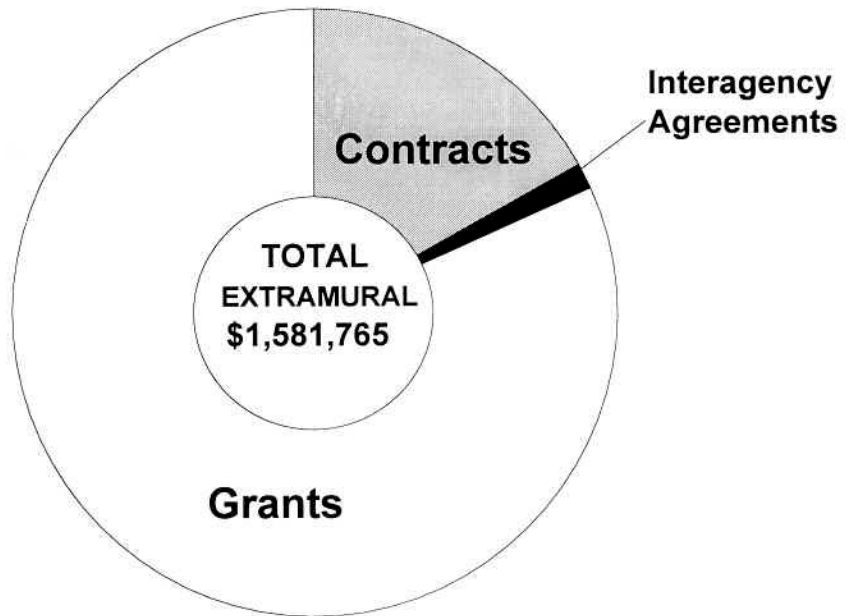


| All Budget Activities | Dollars | Percent of Total |
|--------------------------------------|-------------|------------------|
| Research Programs | \$1,680,921 | 81.0% |
| Resource Development | | |
| Cancer Centers Support | 160,534 | 7.7% |
| Research Manpower Development | 64,086 | 3.1% |
| Construction | 16,822 | 0.8% |
| Cancer Prevention and Control | 153,855 | 7.4% |
| Total NCI | \$2,076,218 | 100.0% |

| Research Budget Activity | Dollars | Percent of Total |
|--------------------------------------|-------------|------------------|
| Epidemiology | \$126,298 | 7.5% |
| Carcinogenesis (Physical & Chemical) | 210,791 | 12.5% |
| Biological Carcinogenesis | 176,382 | 10.5% |
| Nutrition | 56,741 | 3.4% |
| Tumor Biology | 211,824 | 12.6% |
| Immunology | 127,247 | 7.6% |
| Diagnostic Research | 131,969 | 7.9% |
| Preclinical Treatment Research | 281,112 | 16.7% |
| Clinical Treatment Research | 343,229 | 20.4% |
| Rehabilitation Research | 15,328 | 0.9% |
| Total | \$1,680,921 | 100.0% |

Extramural Funds
Fiscal Year 1994

(Dollars in Thousands)



| | Dollars | Percent |
|-------------------------------------|--------------------|---------------|
| Contracts: | | |
| SBIR Contracts | \$1,154 | 0.1% |
| Research Support Contracts | 182,902 | 11.6% |
| Cancer Control Contracts | 84,392 | 5.3% |
| Construction Contracts | 0 | 0.0% |
| Subtotal Contracts | \$268,448 | 17.0% |
| Interagency Agreements | 21,135 | 1.3% |
| Grants: | | |
| Research Project Grants | 934,524 | 59.1% |
| Cancer Centers/SPORES | 158,318 | 10.0% |
| Training Activities | 37,463 | 2.4% |
| Other Research Grants | 107,476 | 6.8% |
| Cancer Control Grants | 37,902 | 2.4% |
| Construction Grants | 16,499 | 1.0% |
| Subtotal Grants | 1,292,182 | 81.7% |
| Total Extramural Funds | 1,581,765 | 100.0% |
| Total Intramural/RMS/Control | 494,453 | |
| Total NCI | \$2,076,218 | |

Total NCI Dollars by Mechanism
Fiscal Year 1994

(Dollars in Thousands)

| | | Number | Amount | Percent of Total |
|--|-----------|--------|-------------|------------------|
| Research Grants: | | | | |
| Research Project Grants: | | | | |
| Traditional | Awards: | 1,914 | \$434,612 | 20.9% |
| Program Projects | | 163 | 184,852 | 8.9% |
| FIRST Awards | | 312 | 32,610 | 1.6% |
| MERIT Awards | | 154 | 48,699 | 2.3% |
| Outstanding Investigator Grants | | 72 | 61,369 | 3.0% |
| RFAs | | 319 | 70,879 | 3.4% |
| Cooperative Agreements | | 232 | 75,444 | 3.6% |
| Shannon Awards | | 9 | 540 | 0.0% |
| Small Grants | | 46 | 2,393 | 0.1% |
| Exploratory/Developmental Grants | | 5 | 353 | 0.0% |
| SBIR Grants | | 179 | 22,773 | 1.1% |
| Subtotal, Research Project Grants | | 3,405 | 934,524 | 45.0% |
| Cancer Centers Grants | | 54 | 136,269 | 6.6% |
| SPOREs | | 9 | 22,049 | 1.1% |
| Subtotal, Centers | | 63 | 158,318 | 7.6% |
| Other Research Grants: | | | | |
| Career Program | | | | |
| RCDA-KO4 | | 19 | 1,235 | 0.1% |
| Clinical Oncology-K12 | | 17 | 2,398 | 0.1% |
| Physician Investigator-K11 | | 50 | 4,110 | 0.2% |
| Preventive Oncology-KO7 | | 23 | 1,884 | 0.1% |
| Clinical Investigator-KO8 | | 54 | 4,186 | 0.2% |
| Minority Faculty Development-K14 | | 24 | 486 | 0.0% |
| Subtotal, Career Program | | 187 | 14,299 | 0.7% |
| Cancer Education Program | | 74 | 8,183 | 0.4% |
| Clinical Cooperative Groups | | 154 | 76,398 | 3.7% |
| Minority Biomedical Support | | 2 | 3,070 | 0.1% |
| Scientific Evaluation | | | 4,197 | 0.2% |
| Instrumentation Grants | | 39 | 742 | 0.0% |
| Continuing Education Grants | | | 171 | 0.0% |
| Conference Grants | | 47 | 416 | 0.0% |
| Subtotal, Other Research Grants | | 503 | 107,476 | 5.2% |
| Subtotal, Research Grants | | 3,971 | 1,200,318 | 57.8% |
| NRSA Fellowships | Trainees: | 1,463 | 37,464 | 1.8% |
| Research and Development Contracts: | | | | |
| R&D Contracts | Awards: | 260 | 204,037 | 9.8% |
| SBIR Contracts | | 7 | 1,154 | 0.1% |
| Subtotal, Contracts | | 267 | 205,191 | 9.9% |
| Intramural Research: | | | | |
| Intramural Research | FTEs: | 1,697 | 251,850 | 12.1% |
| Management Fund | | | 122,874 | 5.9% |
| Subtotal, Intramural Research | | 1,697 | 374,724 | 18.0% |
| Research Management & Support: | | | | |
| Research Management & Support | FTEs: | 516 | 84,310 | 4.1% |
| Management Fund | | | 12,112 | 0.6% |
| Subtotal, RMS | | 516 | 96,422 | 4.6% |
| Cancer Prevention and Control: | | | | |
| Cancer Control Grants | | | 37,902 | 1.8% |
| Cancer Control Contracts | | | 84,392 | 4.1% |
| Inhouse | FTEs: | 169 | 21,568 | 1.0% |
| Management Fund | | | 1,738 | 0.1% |
| Subtotal, Prevention and Control | | 169 | 145,600 | 7.0% |
| Construction | | 5 | 16,499 | 0.8% |
| Total NCI | FTEs: | 2,382 | \$2,076,218 | 100.0% |

**Division Obligations
by Mechanism
Fiscal Year 1994**

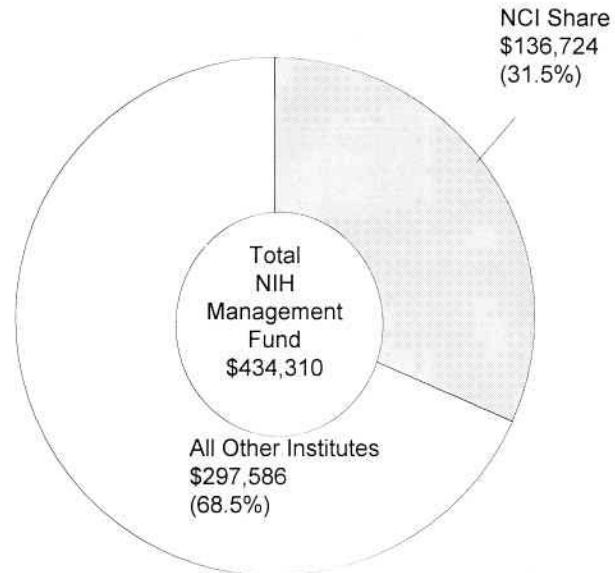
(Dollars in Thousands)

| | DCBDC | DCT | DCE | DCPC | DEA | FCRDC | OD | Research Grants | Program Support(1) | TOTAL NCI |
|--|------------------|------------------|------------------|------------------|-----------------|-----------------|-----------------|------------------|--------------------|--------------------|
| Research Grants: | | | | | | | | | | |
| Research Project Grants | | | | | | | | \$911,751 | | \$911,751 |
| SBIR Grants | | | | | | | | 22,773 | | 22,773 |
| Subtotal, Research Project Grants | | | | | | | | 934,524 | | 934,524 |
| Cancer Centers Grants | \$136,269 | | | | | | | | | 136,269 |
| SPOREs | 21,972 | | | | \$77 | | | | | 22,049 |
| Subtotal, Centers | 158,241 | | | | 77 | | | | | 158,318 |
| Other Research Grants: | | | | | | | | | | |
| Career Program | 13,813 | | | | 486 | | | | | 14,299 |
| Cancer Education Program | 8,183 | | | | | | | | | 8,183 |
| Clinical Cooperative Groups | | \$76,398 | | | | | | | | 76,398 |
| Minority Biomedical Support | | | | | 3,070 | | | | | 3,070 |
| Scientific Evaluation | | | | | 4,197 | | | | | 4,197 |
| Instrumentation Grants | | | | | | | | 742 | | 742 |
| Continuing Ed. Train. Grants | | | | | | | | 171 | | 171 |
| Conference Grants | | | | | | | | 416 | | 416 |
| Subtotal, Other Research Grants | 21,996 | 76,398 | | | 7,753 | | | 1,329 | | 107,476 |
| Subtotal, Research Grants | 180,237 | 76,398 | | | 7,830 | | | 935,853 | | 1,200,318 |
| NRSA Fellowships | 37,336 | | | | 128 | | | | | 37,464 |
| Research and Development Contracts: | | | | | | | | | | |
| R&D Contracts | 7,430 | 59,306 | \$38,013 | \$14,724 | 1,403 | \$55,887 | \$17,128 | | \$10,146 | 204,037 |
| SBIR Contracts | | | | | | | 1,154 | | | 1,154 |
| Subtotal, Contracts | 7,430 | 59,306 | 38,013 | 14,724 | 1,403 | 55,887 | 18,282 | | 10,146 | 205,191 |
| Intramural Research: | | | | | | | | | | |
| Intramural Research | 64,954 | 95,307 | 67,372 | 2,998 | 169 | 11,880 | 6,013 | | 3,157 | 251,850 |
| Management Fund | | | | | | | | | 122,874 | 122,874 |
| Subtotal, Intramural Research | 64,954 | 95,307 | 67,372 | 2,998 | 169 | 11,880 | 6,013 | | 126,031 | 374,724 |
| Research Management & Support: | | | | | | | | | | |
| Research Management & Suppt. Management Fund | 1,969 | | | | 7,909 | 3,000 | 47,094 | | 24,338 | 84,310 |
| Subtotal, RMS | 1,969 | | | | 7,909 | 3,000 | 47,094 | | 36,450 | 96,422 |
| Cancer Prevention and Control: | | | | | | | | | | |
| Cancer Control Grants | | | | 37,902 | | | | | | 37,902 |
| Cancer Control Contracts | | | | 84,392 | | | | | | 84,392 |
| Inhouse | | | | 21,568 | | | | | | 21,568 |
| Management Fund | | | | | | | | | 1,738 | 1,738 |
| Total Prevention & Control | | | | 143,862 | | | | | 1,738 | 145,600 |
| Construction | 15,447 | | | | | 928 | | | 124 | 16,499 |
| Division Totals | \$307,373 | \$231,011 | \$105,385 | \$161,584 | \$17,439 | \$71,695 | \$71,389 | \$935,853 | \$174,489 | \$2,076,218 |

(1) Includes Central Assessments for DHHS-NIH General Expense, Management Fund, and Program Evaluation

**NIH Management Fund
Reimbursement
Fiscal Year 1994**

(Dollars in Thousands)



| DISTRIBUTION OF NCI PAYMENT | | |
|--|------------------|---------------|
| | Dollars | Percent |
| Clinical Center | \$89,790 | 65.7% |
| Division of Research Grants | 4,725 | 3.5% |
| Division of Computer Research and Technology | 6,899 | 5.0% |
| GSA Rental Payments for Space | 5,693 | 4.2% |
| Other Research Services | 29,617 | 21.7% |
| Total, NCI Payment | \$136,724 | 100.0% |

The Management Fund provides for the financing of certain common research and administrative support activities which are required in the operations of NIH:

Clinical Center: Admissions and followup, anesthesiology, diagnostic x-ray, nuclear medicine, clinical pathology, blood bank, rehabilitation medicine, pharmacy, medical records, nursing services, patient nutrition service, housekeeping services, laundry, and social work

Division of Research Grants: initial scientific review of applications, assignment of research grant applications to institutes

Division of Computer Research and Technology: Research and development program in which concepts and methods of computer science are applied to biomedical problems

GSA Rental Payments for Space: building rental including utilities and guard services

Other Research Services: procurement, safety, engineering, biomedical engineering, veterinary resources, and library

Special Sources of Funds

CRADAs

As a result of the Federal Technology Transfer Act of 1986, government laboratories are authorized to enter into Cooperative Research and Development Agreements (CRADAs) with private sector entities. Licensing agreements are usually incorporated into the CRADA document, which addresses patent rights attributable to research supported under the CRADA.

CRADA Receipts Deposited to the U.S. Treasury (dollars in thousands)

| | Carryover from Prior Year | Receipts | Obligations |
|------|---------------------------------|----------|-------------|
| 1990 | \$ 116 | \$ 61 | \$125 |
| 1991 | 52 | 115 | 66 |
| 1992 | 101 | 1,627 | 466 |
| 1993 | 1,262 | 2,509 | 1,582 |
| 1994 | 2,189 | 2,248 | 1,917 |
| 1995 | 2,520 | | |

Royalty Income

NCI retains a portion of the royalty income generated by the patents related to NCI-funded research. A major portion of this royalty income is used to reward employees of the laboratory, to further scientific exchange and for education and training in accordance with the terms of the Act. Receipts are also used to support the costs of processing and collecting royalty income. Support is also provided to cover expenses associated with technology transfer efforts in NCI and NIH.

Royalty Income Funding History (dollars in thousands)

| Years Available | Collections* | Inventor Payments | Other** |
|--------------------|--------------|----------------------|---------|
| 1989/1990 | \$ 813 | \$ 575 | \$ 238 |
| 1990/1991 | 1,452 | 871 | 581 |
| 1991/1992 | 2,084 | 431 | 1,653 |
| 1992/1993 | 2,105 | 451 | 1,654 |
| 1993/1994 | 5,700 | 983 | 4,717 |
| 1994/1995 | 11,244 | 1,235 | 10,009 |

* Does not include assessments by NIH and NTIS.

** To be used for the furtherance of technology transfer

Acquired Immunodeficiency Syndrome (AIDS)

Key Discoveries

The National Cancer Institute has assumed a leading role in Acquired Immunodeficiency Syndrome (AIDS) research since the disease was first recognized in 1981. Because of the research programs and administrative mechanisms already in place, investigators were able to rapidly apply existing methods in drug screening and advances in cancer virus research technology to the study of AIDS. The large scale preparation of HIV-1 in permanent cell lines led to the development of a serological test for AIDS which enabled the detection of AIDS in our nation's blood supply. Detection of the virus in latent form has been established through the *in situ* hybridization method which allowed scientists to detect the virus in brain and blood cells, T lymphocytes and macrophages. Selected recent key discoveries, by NCI investigators include:

- Development, testing and successful clinical trials of the drugs azidothymidine (AZT), dideoxyinosine (ddI) and dideoxycytidine (ddC), confirming their effectiveness as anti-retroviral agents against AIDS.
- Progress in treating children with AIDS has occurred through the rapid introduction of antiretroviral agents into clinical trials. The studies performed by the Pediatric Branch contributed to the licensure of AZT for children in May of 1990 and dideoxyinosine (ddI) in October 1991. The latter, based solely on Pediatric Branch Studies, occurred simultaneously with licensure for adults, a historical event. The Pediatric Branch is currently completing studies of combination regimens to optimize activity (e.g., AZT plus ddI) as well as to offset toxicity (e.g., AZT plus G-CSF and erythropoietin).
- Viral particles are detectable in plasma throughout the early stages of primary infection. The number of viral particles in plasma decrease by up to 200-fold following the initial viremia of primary infection, but increases again as the infection moves from the asymptomatic phase in AIDS-related complex (ARC) to full blown AIDS. The increase in viral particles bears an inverse relationship to CD4 count. Scientists at NCI and elsewhere have adapted Polymerase Chain Reaction (PCR) technology to detect and quantitate the amount of HIV-1 RNA present in plasma. A new adaptation of PCR technology, designated "immuno-PCR", is capable of detecting minute amounts of HIV regulatory proteins (e.g. Tat, Rev) in solution or in tissue. "Immuno-PCR" can be applied to the *in situ* analysis of certain clinical specimens, such as lymph node. Thus, PCR technologies provide the opportunity to correlate HIV protein expression with virulence and pathogenicity in both the laboratory and clinical settings, and may serve as sensitive markers by which to measure response to therapy.
- The ability to provide effective long-term anti-retroviral therapy using single agents for HIV infection is complicated by the emergence of drug-resistant HIV strains. Longitudinal studies of the phenotypic and genotypic changes of HIV strains isolated before and after prolonged therapy with either an alternating regimen of AZT and ddC or ddI alone demonstrate that HIV develops reduced susceptibility to AZT more readily than to ddC and with ddI. A new acyclic purine analog, PMEA, inhibits both HIV RT and DNA polymerase-alpha from CMV and other herpes viruses and may inhibit latent as well as replicating HIV, with perhaps a special activity against the HIV reservoir in monocytes/macrophages. NCI scientists began the Phase I clinical testing of PMEA in combination with AZT in January 1994, in conjunction with assessment of intrinsic or induced HIV resistance to PMEA.
- A recent clinical trial by NCI investigators suggests that the simultaneous administration of AZT and ddI results in higher and more sustained elevations of CD4+ cells over a one year period than alternating drug administration. This difference in clinical activity may relate to differential intracellular drug activation. AZT is preferentially phosphorylated to the active triphosphate form (AZT-TP) in **proliferating** cells. In contrast, the phosphorylation of ddI (to ddATP) and ddC (to ddC-TP) occurs preferentially in **resting** cells. Thus, the data suggest that AZT, ddC and ddI may exert their antiviral

effects depending on the activation state of the target cells; i.e., ddI and ddC likely exert antiviral activity against resting cells, while AZT protects actively growing cells against HIV infection. The combination of AZT+ddI may target both latent and actively replicating pools of virus, providing complementary and possibly synergistic anti-HIV activity.

- Identification through the high-capacity AIDS drug screen of many new compounds which are active against the AIDS virus in tissue culture experiments. These compounds include both synthetic drugs and natural products. Several of these are in the initial phases of development.
- NCI's AIDS Drug Screen has recently uncovered an active compound with an unprecedented mechanism of action, namely the disruption of the highly conserved zinc finger regions of the HIV nucleocapsid protein, p7. The nucleocapsid protein is necessary for the incorporation of the viral RNA genome into intact viral particles and the ultimate packaging of the infectious virions. The ability to block viral reproduction and dissemination by inhibiting the structural and functional integrity of p7 will serve two critical goals: a heightened molecular understanding of the late stages of the viral life cycle, and a template for rational drug design based upon the protein sequence and structure.
- The HIV-1 enzyme reverse transcriptase (RT) is the target for inhibition by many of the currently available anti-retroviral agents, in particular the nucleosides (AZT, ddI, ddC, d4T). Unfortunately, RT is able to undergo mutations that confer resistance to the inhibitory effects of these drugs. Scientists at NCI's Frederick Cancer Research and Development Center have both structural and biochemical data to suggest that the Leu74Val mutation, which causes resistance to ddI, affects the interaction between RT and its nucleic acid substrate. In addition, these scientists continue to define the structure of HIV-1 RT and the complexes formed between RT and its nucleic acid substrates.
- Integration of RT-transcribed HIV DNA into the host genome is facilitated by HIV integrase, an enzyme encoded by the HIV *pol* gene. NCI scientists have devised rapid fluorescent assays that identify both the DNA cleavage reaction and the subsequent integration process in response to purified HIV integrase. The ability to quantitate integrase activity by measuring cleavage-induced changes in fluorescence will also identify agents that block integrase action and thus present a novel molecular target for therapy.
- Determination of the first crystal structure of retroviral protease and its successful use to predict the structure of the HIV protease and substrate using supercomputer methodology. HIV protease is an enzyme whose action is required in the processing of HIV proteins and production of infectious virions. NCI scientists have identified several inhibitors of the HIV protease including KNI-272 which has exhibited potent anti-HIV activity and favorable pharmacokinetics in test animals. In March 1994 NCI scientists began Phase 1 clinical trials of KNI-272.
- Individuals infected with HIV may be asymptomatic for years before progressing to overt AIDS. Since monocytes possess surface CD4 molecules, they can bind and act as a reservoir for HIV in infected individuals. Thus, monocytes in AIDS patients can harbor latent HIV inducible by T cells during an immune response. HIV produced by such monocytes infects T cells leading to viral-induced pathology. In addition to monocytes, NIAID scientists determined that follicular dendritic cells (FDC) also serve as reservoirs for latent HIV infection, sequestering HIV for eventual transmission to CD4+ cells.
- IL-12, produced by macrophages and B cells in response to diverse infectious pathogens, is a natural killer (NK) cell stimulatory factor which activates NK cells *in vitro* and appears to have a significant antitumor effect in tumor-bearing animals. IL-12 drives the differentiation of naive CD4+ T cells into T_H1 cells, thereby promoting cell-mediated immunity. IL-12 may have a special role as an immunostimulant in HIV infection, where both NK cell and T_H1 cell functions are defective. IL-12 may also be able to restore the HIV-related imbalance between T_H1 and T_H2 cells which, in turn, leads to defects in cellular immunity and excessive humoral (antibody) responses.

- The magnitude of CNS disease is often more prominent and the latency period which precedes HIV-related encephalopathy shorter in children than in adults, suggesting that fetal or developing brain cells (in particular, glial cells) may release cytokines capable of activating expression of latent HIV. To address the pathogenesis of neurologic disorders in HIV-1 infected children, NCI scientists have developed an *in vitro* model using a normal fetal olfactory neuroblast cell line, to investigate the potential contributions of direct viral infection and virally-induced cytokines in glial (and perhaps other accessory) cells to neurodevelopmental impairment.
- NCI epidemiologists have played a major role in uncovering the emergence of a new peak of tuberculosis (TB)-associated death in young individuals (ages 20-49) that appears linked to AIDS.
- Recent studies of vaginally-delivered multiple birth cohorts in HIV-infected women demonstrate that HIV transmission is greatest for the first-born infant, suggesting that some component of HIV transmission occurs at the time of the delivery in the cervix or vagina.
- Indeed, about 60 percent of mother-to-infant HIV transmission occurs at the time of birth. On this basis, scientists are designing a clinical trial of inexpensive viricidal solution to cleanse the birth canal to lower the risk of HIV transmission in this setting.
- NCI has established a multi-state AIDS/cancer match registry linking AIDS and cancer registries in five areas of NCI's Surveillance, Epidemiology and End Results (SEER) program (San Francisco, Los Angeles, Atlanta, Detroit and Connecticut) and 10 other sites (New York City and state, New Jersey, Puerto Rico, San Diego, Sacramento, Florida, Illinois, Colorado and Massachusetts). The Registry encompasses about 75 percent of all reported AIDS cases and involves approximately 85,000 matches of individuals with AIDS to cancer registries. This very large data base allows for the first time quantitative estimates of rare as well as common malignancies and provides a framework for determining the role of HIV as a cofactor in the development of diverse malignancies. The registry will also serve to identify patients with concomitant AIDS and cancer from whom tumor tissue and other biologic specimens can be obtained for molecular epidemiologic studies.
- NCI scientists have developed prototype synthetic vaccines consisting of broadly-recognized histocompatibility determinants of T helper cells (so-called "cluster peptides") and a combined site constructed to elicit both cytotoxic T lymphocytes (CTL) and neutralizing antibody. Clinical trials of these constructs are now being launched.
- NCI scientist have constructed novel vaccines comprised of various recombinant and live vectors carrying HIV-1, HIV-2 and SIV antigenic proteins or protein units. These constructs are now being tested in rhesus macaques for their efficacy as initial immunogens, followed by "boosters" using purified native or viral antigens, in eliciting protective immune responses. Recombinant constructs coupling vaccinia virus (poxvirus) vectors to various HIV antigens induce virus-specific cellular and humoral responses in primates. Vaccine constructs coupling adenovirus with HIV-1 MN or IIIB env genes have been shown to elicit both T cell and neutralizing antibody responses, and will be examined in chimpanzees for their protective effects against viral challenge. Finally, influenza recombinants, designed such that the V3 loop is located within a region of the hemagglutinin molecule that is conformationally accessible to antibodies, are being developed as a booster immunogen.
- NCI investigators have put the poly Tat activation region (TAR) which binds to the viral regulatory protein, Tat, into the HIV promoter, thereby inhibiting viral replication. Since binding of Tat to TAR is necessary for RNA expression and viral replication, the polymeric TAR (poly TAR) provides a molecular decoy which inhibits viral replication. Cultures containing the protected cells show a gradual decline in virus production that reaches 90 percent in two months. Six months after infection the protected cell cultures express little detectable virus and are resistant to reinfection. Poly TAR

appears to be an effective antiviral gene that may have eventual clinical application as a gene therapy modality.

- NCI investigators have detected large numbers of KS-like spindle cells in cultures of circulating peripheral blood of HIV+ patients with active KS or at high risk for development of KS. These cells have spindle-shaped morphology and immunophenotypic characteristics of activated endothelial cells, and produce angiogenic factors. The numbers of peripheral blood spindle cells from HIV+ patients with active KS and from those at high risk are increased 78-fold and 18-fold, respectively, over the numbers detectable in HIV- or HIV+ low-risk individuals. The ability to detect such cells may predict susceptibility to develop KS and could serve to monitor the impact of therapeutic and prevention interventions.
- NCI scientists have developed spindle cell strains that provide models of KS for the exploration of new therapeutic approaches. Most recently, a unique KS patient-derived cell line exhibits unlimited cellular life span *in vitro* and aggressive, metastatic behavior *in vivo* in immunosuppressed mice, with formation of highly vascularized tumor nodules. This model mimics KS progression in the human setting and thus may provide an excellent model for dissection of KS pathophysiology and development of targeted antitumor modalities.
- Multiple cytokines (growth factors) with inflammatory, growth-promoting and immunostimulating activities make pivotal contributions to the molecular pathogenesis and clinical phenotype of AIDS-KS. The HIV Tat protein, in particular the biologically active form that is released extracellularly, augments both viral and host gene expression. Basic fibroblast growth factor (b-FGF), an inflammatory cytokine produced by AIDS-KS cells as well as stromal cells, promotes new blood vessel formation (angiogenesis) and wound healing. It has now been shown that b-FGF and Tat interact synergistically to induce proliferation of normal vascular cells and produce KS-like angiogenic lesions in mice *in vivo*. This cooperation is magnified in the HIV+ setting, where b-FGF, extracellular Tat and Tat receptors are present to drive the emergence and aggressive progression of KS.
- A glycoprotein growth factor known as Oncostatin M, derived from activated T-cells, is a potent growth stimulator for AIDS-KS cells. This growth factor is distinct from other important cytokines in AIDS-KS, namely IL-6 and the HIV Tat protein, but binds to the active subunit of the IL-6 receptor. Oncostatin M appears to cause AIDS-KS cell proliferation both directly and in part by enhancing the expression of IL-6 by vascular endothelial cells, and further induces morphologic changes in AIDS-KS cells, namely to the spindle configuration of smooth muscle cells.
- NCI scientists have found a non-cytotoxic bacterial product, a sulfated polysaccharide-peptidoglycan compound (SP-PG) which inhibits the growth and vascular responses, in particular the induction of angiogenesis and hyperpermeability, of AIDS-KS spindle cells *in vitro* and in a nude mouse model.
- The striking production of autostimulatory and angiogenic growth factors by KS cells suggest that these factors should be an important target for therapy. Phase I clinical trials of angiogenesis inhibitors are underway.
- NCI scientists are investigating the antitumor effects of the cytotoxic natural product taxol, a unique tubulin-binding agent, in AIDS-related Kaposi's sarcoma (KS). Of 17 patients treated to date, 50 percent have achieved objective partial responses with roughly 50 percent decreases in number, size and/or nodularity of KS lesions and an additional 40 percent have had stabilization of disease.
- Profound cellular immunodeficiency plays a central role in lymphomagenesis. NCI investigators have found that the most important risk factor determinant for both the AZT- and ddI-treated cohort/s is a CD4 count below the critical level of 50/mm³. In addition, elevated serum levels of IL-6 predict a high risk for NHL development.

- The remarkable occurrence of high-grade B-cell, non-Hodgkin's lymphomas (NHL) has recently emerged as a major sequela of HIV infection, especially in patients who survive other consequences of AIDS in a protracted state of profound immunosuppression. NHLs develop in approximately 10 percent of AIDS patients treated with dideoxynucleosides. NCI investigators have developed a "lymphoma subpanel" comprised of two AIDS lymphoma cell lines including an EBV+ Burkitt's lymphoma, and eight non-AIDS lymphoma cell lines for screening potential therapeutic compounds.
- The severe combined immunodeficiency (SCID) mouse provides a unique model for the study of AIDS-related lymphoma biology and anti-lymphoma drug development. To date, about 500 agents have been examined for *in vitro* antitumor activity against an EBV+ Burkitt's lymphoma derived from an HIV-infected patient. This human tumor cell line has been established as a reproducible *in vivo* model within the SCID mouse. Approximately 18 agents have been evaluated in the *in vivo* model with 3 showing antitumor activity. Further, the CNS involvement of the SCID mouse with this lymphoma provides an opportunity to predict agents that have access to this frequently involved sanctuary in patients. The lymphoma subpanel is being expanded to establish and characterize new AIDS-related lymphoma cell lines, develop "mechanism of action" assays (e.g. IL-6 inhibition, induction of programmed cell death, antiviral effects targeting EBV or other viral cofactors) and define the differential drug sensitivity testing in the *in vivo* SCID model.

**Acquired Immunodeficiency
Syndrome (AIDS)
Funding by Activity
Fiscal Year 1994**

(Dollars in Thousands)

| By Mechanism: | |
|---------------------------------|------------------|
| Research Project Grants | \$27,747 |
| Cancer Center Grants | 3,637 |
| Cooperative Clinical Groups | 323 |
| Conference Grants | 7 |
| Small Grants | 0 |
| R&D Contracts | 68,803 |
| Intramural Research | 104,929 |
| Research Management and Support | 7,422 |
| Total, NCI | <u>\$212,868</u> |

| By Research Thrust: | |
|----------------------------------|------------------|
| Cancer Causation | \$73,737 |
| Detection and Diagnosis Research | 8,785 |
| Treatment Research | 100,281 |
| Cancer Biology | 26,428 |
| Total Research | <u>209,231</u> |
| Cancer Center Grants | <u>3,637</u> |
| Total, NCI | <u>\$212,868</u> |

| By Division: | |
|---|------------------|
| Division of Cancer Biology, Diagnosis and Centers | \$28,772 |
| Division of Cancer Treatment | 74,573 |
| Division of Cancer Etiology | 46,652 |
| Frederick Cancer Research and Development Center | 27,880 |
| Division of Extramural Activities | 1,449 |
| Office of the Director | 5,451 |
| NIH Management Fund* | 28,091 |
| Total, NCI | <u>\$212,868</u> |

**Supports common services shared within the NIH; in AIDS the Management Fund is used principally for support costs associated with NCI's activities at the NIH Clinical Center.*

**Acquired Immunodeficiency
Syndrome (AIDS)
Funding History
Fiscal Years 1983-1994**

(Dollars in Thousands)

| Fiscal Year | NCI Amount | NIH Amount | % NCI To NIH |
|-------------------------|-----------------------|-----------------------|-------------------------|
| 1983 | \$9,790 | \$21,668 | 45% |
| 1984 | 16,627 | 44,121 | 38% |
| 1985 | 26,874 | 63,737 | 42% |
| 1986 | 45,050 | 134,667 | 33% |
| 1987 | 63,755 | 260,907 | 24% |
| 1988 | 89,944 | 473,285 | 19% |
| 1989 | 122,247 | 627,076 | 19% |
| 1990 | 150,304 | 740,509 | 20% |
| 1991 | 160,869 | 799,821 | 20% |
| 1992 (including ADAMHA) | 165,668 | 1,047,294 | 16% |
| 1993 (including ADAMHA) | 173,029 | 1,073,957 | 16% |
| 1994 (including ADAMHA) | 212,868 | 1,298,996 | 16% |

Note:

1983-1991 excludes Alcohol Drug Abuse and Mental Health Administration (ADAMHA), 1992-1994 includes ADAMHA

Extramural
Programs

**Grant and Contract
Awards by State
Fiscal Year 1994**

| State | Grants | | Contracts | | Total NCI |
|----------------------|--------|-------------|-----------|-----------|-------------|
| | Number | Amount | Number | Amount | |
| Alabama | 51 | \$16,166 | 17 | \$12,056 | \$28,222 |
| Alaska | 4 | 802 | 1 | 64 | 866 |
| Arizona | 50 | 22,573 | 1 | 199 | 22,772 |
| Arkansas | 10 | 2,182 | | | 2,182 |
| California | 583 | 181,066 | 29 | 12,523 | 193,589 |
| Colorado | 70 | 23,192 | 6 | 3,059 | 26,251 |
| Connecticut | 71 | 19,935 | 4 | 2,332 | 22,267 |
| Delaware | 1 | 259 | | | 259 |
| District of Columbia | 71 | 22,984 | 9 | 2,150 | 25,134 |
| Florida | 61 | 14,057 | 6 | 1,643 | 15,700 |
| Georgia | 30 | 5,300 | 11 | 3,393 | 8,693 |
| Hawaii | 24 | 9,117 | 3 | 1,691 | 10,808 |
| Idaho | | | | | |
| Illinois | 148 | 36,688 | 14 | 5,331 | 42,019 |
| Indiana | 26 | 6,605 | 5 | 1,280 | 7,885 |
| Iowa | 22 | 3,498 | 4 | 2,998 | 6,496 |
| Kansas | 21 | 4,184 | 4 | 1,891 | 6,075 |
| Kentucky | 29 | 3,494 | 5 | 2,501 | 5,995 |
| Louisiana | 18 | 3,387 | 1 | 129 | 3,516 |
| Maine | 10 | 3,086 | 1 | 806 | 3,892 |
| Maryland | 168 | 52,911 | 109 | 112,320 | 165,231 |
| Massachusetts | 441 | 140,099 | 15 | 5,675 | 145,774 |
| Michigan | 168 | 36,795 | 12 | 8,545 | 45,340 |
| Minnesota | 95 | 30,633 | 7 | 3,488 | 34,121 |
| Mississippi | 5 | 507 | | | 507 |
| Missouri | 64 | 13,573 | 9 | 4,726 | 18,299 |
| Montana | 2 | 207 | | | 207 |
| Nebraska | 24 | 5,542 | | | 5,542 |
| Nevada | 5 | 631 | | | 631 |
| New Hampshire | 34 | 12,732 | 1 | 60 | 12,792 |
| New Jersey | 54 | 13,150 | 4 | 3,704 | 16,854 |
| New Mexico | 15 | 5,665 | 4 | 2,410 | 8,075 |
| New York | 470 | 153,035 | 23 | 11,348 | 164,383 |
| North Carolina | 177 | 52,335 | 16 | 10,224 | 62,559 |
| North Dakota | 6 | 728 | | | 728 |
| Ohio | 126 | 29,056 | 4 | 4,129 | 33,185 |
| Oklahoma | 11 | 1,514 | | | 1,514 |
| Oregon | 23 | 5,815 | 3 | 870 | 6,685 |
| Pennsylvania | 341 | 101,951 | 8 | 4,772 | 106,723 |
| Rhode Island | 34 | 8,927 | 1 | 844 | 9,771 |
| South Carolina | 18 | 3,229 | 1 | 948 | 4,177 |
| South Dakota | 3 | 490 | | | 490 |
| Tennessee | 89 | 24,242 | 4 | 1,524 | 25,766 |
| Texas | 300 | 86,150 | 14 | 5,497 | 91,647 |
| Utah | 33 | 9,635 | 5 | 1,363 | 10,998 |
| Vermont | 16 | 4,310 | 1 | 274 | 4,584 |
| Virginia | 58 | 19,494 | 15 | 37,769 | 57,263 |
| Washington | 171 | 64,377 | 9 | 5,396 | 69,773 |
| West Virginia | 9 | 1,595 | 3 | 1,736 | 3,331 |
| Wisconsin | 95 | 25,914 | 9 | 4,126 | 30,040 |
| Wyoming | | | | | |
| Total | 4,355 | 1,283,817 | 398 | 285,794 | 1,569,611 |
| Puerto Rico | 1 | 303 | | | 303 |
| US Virgin Islands | 1 | 101 | | | 101 |
| Total | 4,357 | \$1,284,221 | 398 | \$285,794 | \$1,570,015 |

**NCI Foreign Research
Grants and Contracts
Fiscal Year 1994**

(Dollars in Thousands)

| Country | Grant | | Contract | | Total NCI Awards | Percent of Total Dollars Awarded |
|--------------------------|-----------|----------------|-----------|----------------|------------------|----------------------------------|
| | Number | Amount | Number | Amount | | |
| Australia | 7 | \$747 | | | \$747 | 6.4% |
| Belgium | 2 | 438 | | | 438 | 3.7% |
| Canada | 22 | 2,101 | 1 | \$79 | 2,180 | 18.5% |
| China | | | 4 | 704 | 704 | 6.0% |
| Costa Rica | | | 1 | 238 | 238 | 2.0% |
| Denmark | 2 | 337 | 2 | 433 | 771 | 6.6% |
| Finland | 1 | 104 | 2 | 668 | 772 | 6.6% |
| France | 2 | 504 | | | 504 | 4.3% |
| Ghana | | | 1 | 68 | 68 | 0.6% |
| Israel | 4 | 622 | | | 622 | 5.3% |
| Italy | 2 | 583 | | | 583 | 5.0% |
| Jamaica | | | 2 | 726 | 726 | 6.2% |
| Japan | | | 1 | 66 | 66 | 0.6% |
| Netherlands | 1 | 102 | | | 102 | 0.9% |
| New Zealand | | | 2 | 760 | 760 | 6.5% |
| Republic of South Africa | 1 | 61 | | | 61 | 0.5% |
| Sweden | 5 | 951 | 2 | 357 | 1,308 | 11.1% |
| Switzerland | 1 | 24 | | | 24 | 0.2% |
| Tanzania | | | 1 | 20 | 20 | 0.2% |
| Trinidad | | | 2 | 723 | 723 | 6.2% |
| United Kingdom | 6 | 338 | | | 338 | 2.9% |
| Total Foreign | 56 | \$6,911 | 21 | \$4,843 | \$11,754 | 100.0% |

**Institutions Receiving More than
\$10,000,000 in NCI Support
Fiscal Year 1994**

(Dollars in Thousands)

| State | Institution | Grants | Contracts | Construction | Total NCI | |
|-----------------------|--|-------------------------------------|-----------|--------------|-----------|--------|
| Alabama | University of Alabama System | \$11,126 | \$4,420 | | \$15,546 | |
| | Southern Research Institute | 3,880 | 7,636 | | 11,516 | |
| Arizona | University of Arizona | 18,262 | 199 | \$1,570 | 20,031 | |
| California | University of California | 76,198 | 1,874 | | 78,072 | |
| | Stanford University | 21,053 | | | 21,053 | |
| | University of Southern California | 14,284 | 2,485 | 67 | 16,836 | |
| | Scripps Research Institute | 10,650 | | | 10,650 | |
| Colorado | University of Colorado System | 9,368 | 977 | | 10,345 | |
| Connecticut | Yale University | 18,982 | 879 | | 19,861 | |
| District of Columbia | Georgetown University | 12,767 | 717 | | 13,484 | |
| Illinois | University of Chicago | 12,654 | 105 | | 12,759 | |
| | University of Illinois System | 9,094 | 2,704 | | 11,798 | |
| Maryland | Johns Hopkins University | 37,773 | 1,236 | 1,570 | 40,579 | |
| | Organon Teknika Corporation | | 31,910 | | 31,910 | |
| | Westat, Inc. | | 15,030 | | 15,030 | |
| Massachusetts | Dana-Farber Cancer Institute | 29,865 | | 1,970 | 31,835 | |
| | Harvard University | 17,813 | 175 | | 17,988 | |
| | Massachusetts General Hospital | 13,791 | | 7,400 | 21,191 | |
| | Brigham and Women's Hospital | 16,839 | | | 16,839 | |
| | Massachusetts Institute of Technology | 10,026 | | | 10,026 | |
| Michigan | University of Michigan at Ann Arbor | 19,157 | | | 19,157 | |
| Minnesota | University of Minnesota | 16,179 | 1,756 | | 17,935 | |
| | Mayo Foundation | 11,809 | 631 | | 12,440 | |
| Missouri | Washington University | 9,559 | 776 | | 10,335 | |
| New Hampshire | Dartmouth College | 12,711 | 60 | | 12,771 | |
| New York | Memorial Sloan-Kettering | 30,969 | 2,756 | | 33,725 | |
| | Columbia University | 15,601 | | | 15,601 | |
| | New York University | 14,632 | | | 14,632 | |
| | Yeshiva University | 13,033 | | | 13,033 | |
| | Cold Spring Harbor Laboratory | 10,256 | | | 10,256 | |
| | American Health Foundation | 9,344 | 781 | | 10,125 | |
| | New York State Dept. of Health | 16,010 | 2,709 | | 18,719 | |
| | North Carolina | University of North Carolina System | 21,856 | 322 | | 22,178 |
| | | Duke University | 21,683 | 930 | | 22,613 |
| | Ohio | Case Western Reserve University | 13,098 | 1,080 | | 14,178 |
| Ohio State University | | 9,260 | 1,140 | | 10,400 | |
| Pennsylvania | University of Pittsburgh | 23,461 | 1,920 | | 25,381 | |
| | University of Pennsylvania | 16,510 | 110 | | 16,620 | |
| | Fox Chase Cancer Center | 21,979 | 2,730 | | 24,709 | |
| | Thomas Jefferson University | 13,036 | | | 13,036 | |
| Tennessee | St. Jude Children's Research Hospital | 12,665 | | | 12,665 | |
| Texas | University of Texas System | 57,217 | 3,809 | | 61,026 | |
| | Cancer Therapy and Research Center | 15,607 | | 900 | 16,507 | |
| Utah | Utah State Higher Education System | 9,454 | 1,363 | | 10,817 | |
| Virginia | Dyncorp | | 30,378 | | 30,378 | |
| Washington | Fred Hutchinson Cancer Research Center | 43,236 | 4,071 | | 47,307 | |
| | University of Washington | 14,214 | 22 | | 14,236 | |
| Wisconsin | University of Wisconsin System | 22,034 | 1,784 | | 23,818 | |
| Total | | \$838,995 | \$129,475 | \$13,477 | \$981,947 | |

Cancer Centers Funding History

| Fiscal Year | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 |
|----------------|---------------|---------------|---------------|---------------|---------------|---------------|
| Center Support | \$101,127,000 | \$105,268,000 | \$110,481,000 | \$127,351,000 | \$123,930,000 | \$136,269,000 |
| Annual Growth | 0.7% | 4.1% | 5.0% | 15.3% | -2.7% | 10% |

Cancer centers supported by the NCI multidisciplinary research programs at academic and other organizations are one of the key elements of the research infrastructure for cancer research. As a group, they are engaged in all aspects of cancer research, including basic, clinical, and cancer control research. Cancer Centers also serve as a stable resource for training new cancer investigators. Of the 54 cancer center support grants (CCSG) awarded in FY 1994, 12 were to basic laboratory centers, 1 was to a consortium center, 15 were to clinical centers, and 26 were to comprehensive centers. In addition, the 14 P20 Cancer Center Planning Grants which were funded in FY 1992 and FY 1993, received continuing support in FY 1994. Cancer Center Planning Grants were initiated in FY 1992 to increase geographic distribution of cancer centers in underrepresented areas of the country.

New funding initiatives were specifically designed to strengthen the Cancer Centers Program and promote the fulfillment of its mission. Highlights of the past year include the following: (1) P20 planning grants for the development of breast cancer programs in NCI-designated cancer centers were awarded with \$4.0 million. Additional funds from the National Institute on Aging and the National Institute for Environmental Health Sciences provided further support, allowing co-funding of a number of applications whose research emphasis was of high programmatic priority to the co-sponsoring Institutes; (2) funds were awarded to 16 cancer centers to further the development of solid and enduring research programs in the area of cancer prevention and control. Funds are intended to support the recruitment of new investigators in the prevention and control research tenure track (or equivalent positions) or for the support of pilot projects; (3) among the P20 breast cancer program awards, four grants specifically incorporated a major focus on environmental carcinogenesis and epidemiology consistent with the Long Island Breast Cancer Study, a major study initiated in response to a congressional mandate; (4) funds were awarded to 35 institutions, representing 28 established cancer centers and seven centers with planning grants, for the purchase of either a single piece of equipment or an integrated set of equipment items to be used for a single purpose; (5) a revised policy on the inclusion of women and minorities in clinical trials, issued in March, 1994, has brought heightened attention to this issue in competing CCSG applications; (6) institutions that are not current recipients of CCSGs, in addition to institutions that were awarded planning grants in 1992, submitted competing applications to become NCI-designated cancer centers; (7) one new CCSG was awarded in FY 1994, to the University of California, Irvine; (8) under the auspices of a special chartered committee, the revised guidelines for designation as a NCI Comprehensive Cancer Center, implemented in 1993, have now been applied to the review of ten centers; (9) pilot projects in high-priority research areas of prostate, ovarian, breast, and cervical cancer; gene therapy; vaccine development; AIDS-related cancer; and Kaposi's sarcoma, initiated in FY 1992, are coming to completion while others are being initiated reflecting continuing interest of cancer centers in these research areas; (10) workshops for Cancer Center Directors and P20 Planning Grant Directors.

The P20 Planning Grant for Breast Cancer Research Programs was activated in FY 1994 and was co-sponsored by the NCI, the National Institute on Aging, and the National Institute for Environmental Health Sciences. Through this RFA, Cancer Centers were invited to develop broad, multidisciplinary research programs including basic, clinical and prevention and control approaches to breast cancer research. The RFA emphasized inclusion of research not only on breast cancer in young women and populations of women with higher rates of breast cancer, but also environmental influences on breast cancer. Eighteen grants were funded with future year commitments. Another nine grants were funded for one year.

As a way to further encourage the representation of cancer centers in underserved areas, an RFA was again issued in FY 1994 to announce the availability of planning and development grants for cancer centers for this purpose. This initiative was intended to provide current P20 recipients an opportunity to continue their planning and development activities or for new institutions to begin similar ventures. In addition to basic cancer research, these centers are expected to emphasize clinical and prevention/control research that will ultimately impact on the populations in their regions, paying particular attention to minority, rural, and other underserved populations. Approximately three to five awards are expected to be made in FY 1995 in response to this initiative.

Since 1978, the NCI has recognized a category of cancer centers designated as Comprehensive, and so termed because of the broad array of cancer research, training, information, and outreach services they provide to their communities. Comprehensive Guidelines, initially issued in 1990 and revised in 1993, refined and clarified the concept of an NCI-designated comprehensive cancer center, the application procedures and the peer review criteria that centers were to use to attain and renew this designation. The revised guidelines introduced greater rigor and consistency to the process of achieving comprehensive status, requiring meritorious achievement in the following review criteria.

Criteria for Comprehensiveness

Together with scientific excellence and leadership, the essential characteristics of a comprehensive cancer center include:

- 1) **Basic Laboratory Research:** A critical mass of integrated personnel, facilities and peer-reviewed support for interdisciplinary basic research is essential in a comprehensive cancer center.
- 2) **Basic/Clinical Research Linkage:** A comprehensive cancer center should facilitate the transfer of exciting laboratory discoveries to innovative clinical applications, including clinical treatment and prevention.
- 3) **Clinical Research:** A significant clinical research program utilizing patient resources of the institution and its region is essential.
- 4) **High-Priority Clinical Trial Research:** Comprehensive centers should participate significantly in clinical trials that have been accorded high-priority status by the NCI, *unless* the center is participating in trials testing competing hypotheses for the same disease site.
- 5) **Cancer Prevention and Control Research:** Comprehensive cancer centers are expected to have peer-reviewed research in cancer prevention and control and to have planned or ongoing involvement in cancer control on a regional and national basis.
- 6) **Education, Training and Provision of Updates on Current Technology:** It is essential that a comprehensive center be a focal point for clinical and research training, including state-of-the-art research and technology, for health care professionals locally and within the region.
- 7) **Information Services:** A comprehensive cancer center should have an established patient education program and the ability to provide patients and their families with up-to-date information on local as well as national resources that may be needed. In addition, the center should participate in its region's Cancer Information Service.
- 8) **Community Service and Outreach:** A comprehensive cancer center should define the community it serves, take steps to identify cancer issues and problems in this community, and carry out appropriate outreach programs addressing these concerns including cancer prevention and control activities.

Cancer Centers by State (P30 Core Grants)

| State | Grantee Institution | Type | Awarded |
|----------------------|---|---------------|---------------|
| Alabama | University of Alabama at Birmingham | Comprehensive | \$3,780,307 |
| Arizona | University of Arizona | Comprehensive | 1,808,420 |
| California | Beckman Research Institute/City of Hope | Clinical | 1,336,446 |
| | La Jolla Cancer Research Foundation | Lab/Basic | 1,355,570 |
| | Salk Institute for Biological Sciences | Lab/Basic | 1,641,560 |
| | University of California at Los Angeles | Comprehensive | 3,036,287 |
| | University of California at San Diego | Clinical | 1,318,854 |
| | University of California, Irvine Clinical Cancer Center | Clinical | 1,070,140 |
| | University of Southern California | Comprehensive | 3,400,597 |
| Colorado | University of Colorado Health Sciences Center | Clinical | 2,178,677 |
| Connecticut | Yale University | Comprehensive | 2,209,458 |
| District of Columbia | Georgetown University | Comprehensive | 1,846,778 |
| Florida | University of Miami | Comprehensive | 2,160,259 |
| Illinois | Northwestern University | Clinical | 1,271,473 |
| | University of Chicago | Clinical | 2,032,340 |
| Indiana | Purdue University West Lafayette | Lab/Basic | 637,777 |
| Maine | Jackson Laboratory | Lab/Basic | 1,318,447 |
| Maryland | Johns Hopkins University | Comprehensive | 4,393,104 |
| Massachusetts | Dana-Farber Cancer Institute | Comprehensive | 3,350,714 |
| | Massachusetts Institute of Technology | Lab/Basic | 1,732,849 |
| Michigan | University of Michigan at Ann Arbor | Comprehensive | 2,074,698 |
| | Wayne State University | Comprehensive | 1,091,822 |
| Minnesota | Mayo Foundation | Clinical | 2,192,496 |
| Nebraska | University of Nebraska Medical Center | Lab/Basic | 936,406 |
| New Hampshire | Dartmouth College | Comprehensive | 1,697,631 |
| New York | Cold Spring Harbor Laboratory | Lab/Basic | 2,754,715 |
| | Columbia University New York | Clinical | 3,131,341 |
| | Kaplan Comprehensive Cancer Center/NYU | Comprehensive | 3,374,087 |
| | Roswell Park Memorial Institute | Comprehensive | 1,810,838 |
| | Memorial Sloan-Kettering | Comprehensive | 5,561,534 |
| | University of Rochester | Clinical | 2,511,802 |
| | American Health Foundation | Lab/Basic | 2,060,812 |
| | Albert Einstein College of Medicine | Clinical | 3,926,496 |
| North Carolina | Duke University | Comprehensive | 3,670,729 |
| | University of North Carolina Chapel Hill | Comprehensive | 2,336,982 |
| | Wake Forest University/Bowman Gray Sch. of Medicine | Comprehensive | 1,429,475 |
| Ohio | Case Western Reserve University | Clinical | 1,348,871 |
| | Ohio State University | Comprehensive | 2,897,712 |
| Pennsylvania | Fox Chase Cancer Center | Comprehensive | 6,671,045 |
| | Temple University | Lab/Basic | 995,441 |
| | University of Pennsylvania | Comprehensive | 2,200,528 |
| | University of Pittsburgh | Comprehensive | 1,657,260 |
| | Wistar Institute of Anatomy and Biology | Lab/Basic | 2,832,805 |
| Tennessee | St. Jude Children's Research Hospital | Clinical | 3,615,702 |
| | Drew-Meharry-Morehouse Consortium Cancer Center | Consortium | 1,149,312 |
| Texas | San Antonio Cancer Institute | Clinical | 1,820,605 |
| | M.D. Anderson Cancer Center/Univ. of Texas | Comprehensive | 2,272,590 |
| Utah | University of Utah | Clinical | 1,254,148 |
| Vermont | University of Vermont | Comprehensive | 1,038,433 |
| Virginia | University of Virginia | Lab/Basic | 695,616 |
| | Medical College of Virginia/VCU | Clinical | 850,250 |
| Washington | Fred Hutchinson Cancer Research Center | Comprehensive | 5,533,841 |
| Wisconsin | McArdle Laboratory for Cancer Research | Lab/Basic | 2,548,268 |
| | University of Wisconsin Madison | Comprehensive | 2,812,287 |
| Total P30s | | 54 | 124,636,635 |
| P20 Planning Grants | | | 11,632,365 |
| Total Cancer Centers | | | \$136,269,000 |

Specialized Programs of Research Excellence SPORES

In 1992, the NCI established the Specialized Programs of Research Excellence (SPORES) to promote interdisciplinary research and to speed the bidirectional exchange between basic and clinical science in order to move basic research findings from the laboratory to applied settings involving patients and populations. The ultimate goal of the SPORE program is to bring novel ideas that have the potential to reduce cancer incidence and mortality, improve survival, and to improve the quality of life to clinical care settings.

Laboratory and clinical scientists work collaboratively in planning, designing and implementing research programs that impact on cancer prevention, detection, diagnosis, treatment and control. To facilitate this research, each SPORE develops and maintains specialized resources that benefit all scientists working on the specific cancer site, as well as SPORE scientists. An additional SPORE element is a career development program that recruits scientists both within and outside the SPORE institution to enlarge the cadre of laboratory and clinical scientists dedicated to translational research on human cancer. SPORES meet annually to share data, assess research progress, identify new research opportunities and establish priorities for research most likely to reduce incidence and mortality and to increase survival.

In 1994, NCI funded a total of 9 SPORES and 24 P20 Planning Grants for a total of \$22,049,000. SPORES are funded through both the P50 and P20 mechanisms. Nine institutions received full support as P50 SPORES. Twelve P20s were awarded to institutions to conduct feasibility studies to determine whether they would qualify to become fully funded SPORE institutions. In the upcoming years, NCI may increase the use of the SPORE mechanism to include funding for other major cancer sites.

| <u>Site</u> | <u>Type</u> | <u>Number of Awards</u> | <u>Amount of Funding</u> |
|---------------------|-------------------------------|-------------------------|--------------------------|
| Breast | P50 | 4 | \$7,969,000 |
| | P20 | 6 | 773,000 |
| | Total Breast | 10 | 8,742,000 |
| Gastrointestinal | P50 | 1 | 1,540,000 |
| | Total Gastrointestinal | 1 | 1,540,000 |
| Lung | P50 | 2 | 4,147,000 |
| | P20 | 2 | 439,000 |
| | Total Lung | 4 | 4,586,000 |
| Prostate | P50 | 2 | 5,191,000 |
| | P20 | 5 | 617,000 |
| | Total Prostate | 7 | 5,808,000 |
| Brain Tumor | P20 | 11 | 1,373,000 |
| | Total Brain Tumor | 11 | 1,373,000 |
| 78 | P20 | 24 | 18,847,000 |
| | P50 | 9 | 3,202,000 |
| Total SPORES | | | \$22,049,000 |

**Total Research
Project Grants
Fiscal Years 1988-1994**

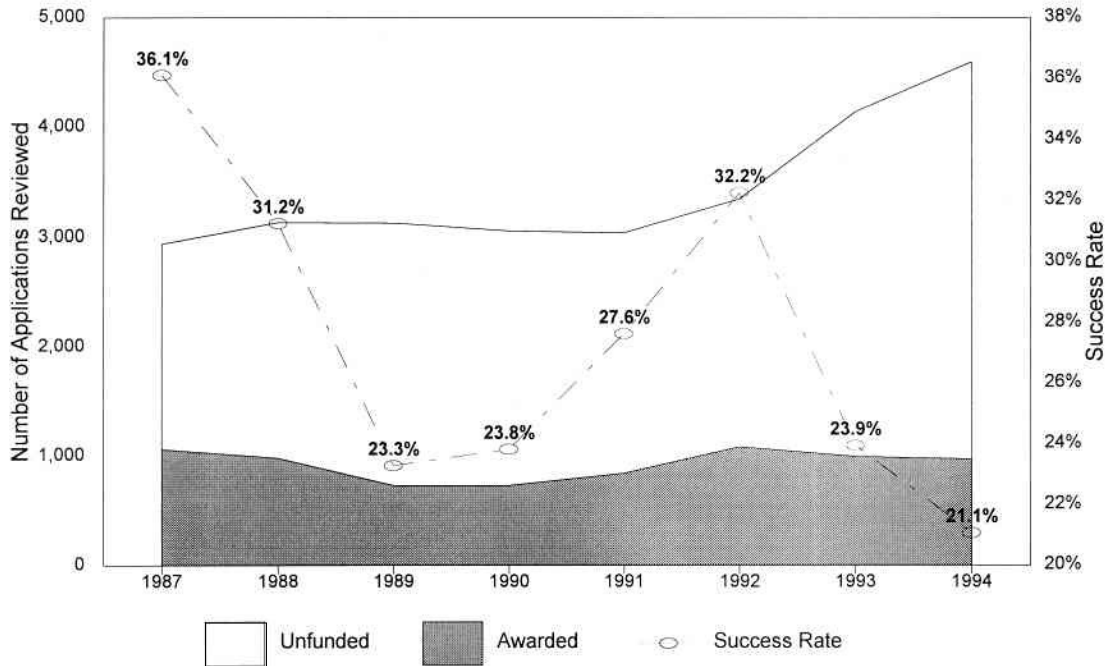
(Dollars in Thousands)

| Fiscal Year | Type Awarded | Requested | | Awarded | | Success Rate |
|-------------------|-----------------------|-----------|-----------|--------------|----------------|--------------|
| | | No. | Amt. | No. | Amt. | |
| 1988 | Competing | | | | | |
| | New..... | 2,167 | \$419,638 | 470 | \$83,083 | |
| | Renewal..... | 951 | 262,675 | 506 | 122,229 | |
| | Board Supplement..... | 15 | 1,717 | 3 | 66 | |
| | Subtotal..... | 3,133 | 684,030 | 979 | 205,378 | 31.2% |
| Noncompeting..... | | | 2,078 | 460,025 | | |
| Total..... | | | | 3,057 | 665,403 | |
| 1989 | Competing | | | | | |
| | New..... | 2,290 | \$474,978 | 402 | \$73,081 | |
| | Renewal..... | 823 | 246,172 | 324 | 85,645 | |
| | Board Supplement..... | 14 | 2,883 | 2 | 49 | |
| | Subtotal..... | 3,127 | 724,033 | 728 | 158,775 | 23.3% |
| Noncompeting..... | | | 2,374 | 564,234 | | |
| Total..... | | | | 3,102 | 723,009 | |
| 1990 | Competing | | | | | |
| | New..... | 2,193 | \$527,256 | 421 | \$82,656 | |
| | Renewal..... | 849 | 278,541 | 302 | 87,497 | |
| | Board Supplement..... | 15 | 2,837 | 5 | 991 | |
| | Subtotal..... | 3,057 | 808,634 | 728 | 171,144 | 23.8% |
| Noncompeting..... | | | 2,288 | 568,336 | | |
| Total..... | | | | 3,016 | 739,480 | |
| 1991 | Competing | | | | | |
| | New..... | 2,195 | \$512,665 | 513 | \$102,364 | |
| | Renewal..... | 837 | 286,858 | 323 | 94,231 | |
| | Board Supplement..... | 8 | 1,161 | 4 | 421 | |
| | Subtotal..... | 3,040 | 800,684 | 840 | 197,016 | 27.6% |
| Noncompeting..... | | | 2,207 | 594,532 | | |
| Total..... | | | | 3,047 | 791,548 | |
| 1992 | Competing | | | | | |
| | New..... | 2,508 | \$612,369 | 664 | \$119,091 | |
| | Renewal..... | 815 | 332,428 | 398 | 133,413 | |
| | Board Supplement..... | 23 | 3,704 | 17 | 1,347 | |
| | Subtotal..... | 3,346 | 948,501 | 1,079 | 253,851 | 32.2% |
| Noncompeting..... | | | 2,231 | 620,006 | | |
| Total..... | | | | 3,310 | 873,857 | |
| 1993 | Competing | | | | | |
| | New..... | 3,173 | \$746,912 | 644 | \$114,227 | |
| | Renewal..... | 891 | 328,657 | 340 | 107,949 | |
| | Board Supplement..... | 75 | 8,554 | 7 | 1,698 | |
| | Subtotal..... | 4,139 | 1,084,123 | 991 | 223,874 | 23.9% |
| Noncompeting..... | | | 2,346 | 692,436 | | |
| Total..... | | | | 3,337 | 916,310 | |
| 1994 | Competing | | | | | |
| | New..... | 3,643 | \$787,824 | 657 | \$118,403 | |
| | Renewal..... | 935 | 342,068 | 308 | 110,723 | |
| | Board Supplement..... | 20 | 3,311 | 4 | 733 | |
| | Subtotal..... | 4,598 | 1,133,203 | 969 | 229,859 | 21.1% |
| Noncompeting..... | | | 2,436 | 704,665 | | |
| Total..... | | | | 3,405 | 934,524 | |

Note: RPGs include R01 traditional grants, P01 program projects, R23 new investigator research awards, R29 FIRST awards, R35 Outstanding Investigator Grants, R37 MERIT awards, U01 Cooperative Agreement awards, R01 and U01 awards of Request for Applications, R03 small grants, R21 Exploratory/Developmental Grants and R43/R44 Small Business Innovative Research awards.
Success rate is the number of awarded grants divided by the number of awards requested. Requested data from 1986 through 1990 includes all submitted applications. Beginning in 1991, the requested data excludes applications not recommended for further review by DRG. 1993 requested data was updated since printing the 1993 Factbook.

**Success Rate:
Fiscal Years 1987-1994**

RPG Success Rate

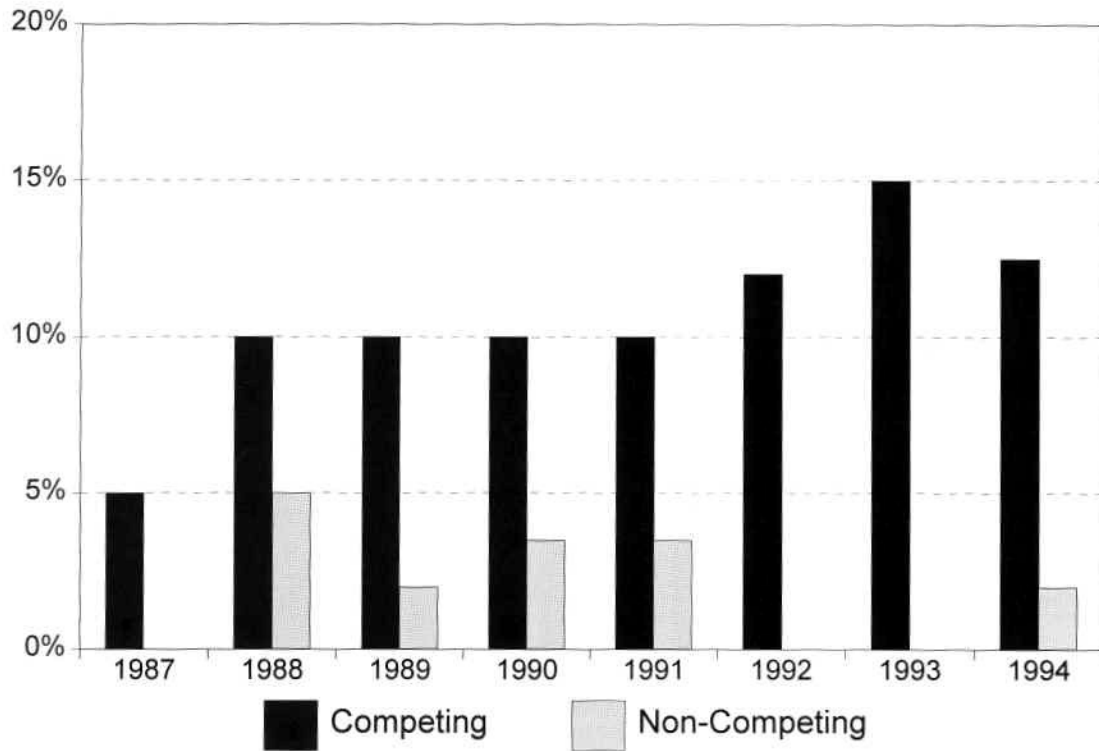


| RPG Applications | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 |
|----------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Annual % Change: | | | | | | | | |
| in Awarded | | -8% | -26% | 0% | 15% | 28% | -8% | -2% |
| in Success Rate Base | | 7% | 0% | -2% | -1% | 10% | 24% | 11% |
| in Success Rate | | -13% | -25% | 2% | 16% | 17% | -26% | -12% |
| Numbers of RPGs: | | | | | | | | |
| Awarded | 1061 | 979 | 728 | 728 | 840 | 1079 | 991 | 969 |
| Success Rate Base | 2939 | 3133 | 3127 | 3057 | 3040 | 3346 | 4139 | 4598 |
| Success Rate | 36.1% | 31.2% | 23.3% | 23.8% | 27.6% | 32.2% | 23.9% | 21.1% |

The success rate base is the number of applications reviewed.

The success rate is the number awarded as a percent of the success rate base (the number of applications reviewed)

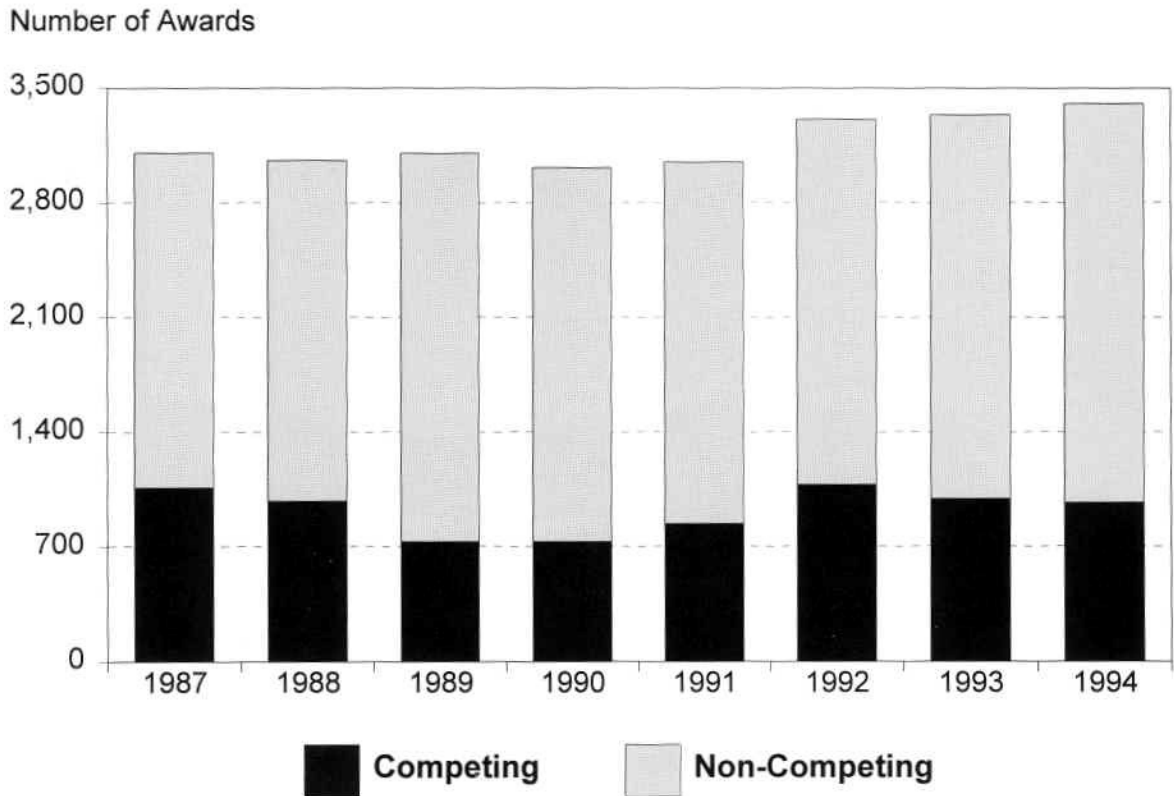
**Research Project Grants
Adjustments from Recommended Levels
Fiscal Years 1987-1994**



| TYPE | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 |
|---------------|------|-------|-------|-------|-------|-------|-------|-------|
| Competing | 5.0% | 10.0% | 10.0% | 10.0% | 10.0% | 12.0% | 15.0% | 12.5% |
| Non-Competing | 0.0% | 5.0% | 2.0% | 3.5% | 3.5% | 0.0% | 0.0% | 2.0% |

NOTE: Future year (non-competing) approved amounts are reduced by the average percentage reductions applied during the competing grant cycle. The percent reductions shown are taken against this adjusted base. FY 1987, 1992 and 1993 non-competing awards were paid at the committed level.

**Research Project Grants
Number of Awards
Fiscal Years 1987-1994**



| TYPE | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 |
|---------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Competing | 1,061 | 979 | 728 | 728 | 840 | 1,079 | 991 | 969 |
| Non-Competing | 2,042 | 2,078 | 2,374 | 2,288 | 2,207 | 2,231 | 2,346 | 2,436 |
| Total | 3,103 | 3,057 | 3,102 | 3,016 | 3,047 | 3,310 | 3,337 | 3,405 |

Research Project Grants

(Dollars in Thousands)

Awarded

History by Activity

Fiscal Years 1989-1994

| TYPE | 1989 | | 1990 | | 1991 | | 1992 | | 1993 | | 1994 | |
|--------------|--------------|------------------|--------------|------------------|--------------|------------------|--------------|------------------|--------------|------------------|--------------|------------------|
| | Number | Amount | Number | Amount | Number | Amount | Number | Amount | Number | Amount | Number | Amount |
| RO1 | 2,239 | \$377,164 | 2,068 | \$371,225 | 1,949 | \$381,932 | 2,050 | \$424,954 | 1,955 | \$430,203 | 1,914 | \$434,612 |
| PO1 | 165 | 188,015 | 162 | 185,130 | 165 | 190,470 | 183 | 205,330 | 176 | 202,852 | 163 | 184,852 |
| R35 | 75 | 52,973 | 78 | 57,857 | 84 | 62,137 | 76 | 59,878 | 75 | 61,337 | 72 | 61,369 |
| R37 | 132 | 32,353 | 153 | 39,264 | 163 | 43,687 | 162 | 47,414 | 166 | 51,633 | 154 | 48,699 |
| UO1 | 70 | 20,939 | 87 | 31,145 | 85 | 32,431 | 123 | 44,171 | 171 | 56,199 | 232 | 75,444 |
| R29 | 232 | 21,244 | 280 | 25,547 | 316 | 29,494 | 309 | 29,726 | 291 | 29,053 | 312 | 32,610 |
| RFA | 108 | 18,884 | 101 | 17,335 | 154 | 37,435 | 208 | 45,107 | 282 | 63,267 | 319 | 70,879 |
| R43-R44 | 79 | 11,332 | 87 | 11,977 | 131 | 13,962 | 199 | 17,277 | 215 | 20,401 | 179 | 22,773 |
| R03 | | | | | | | | | | | 46 | 2,393 |
| R21 | | | | | | | | | | | 5 | 353 |
| R23 | 2 | 105 | | | | | | | | | | |
| R55 | | | | | | | | | 6 | 1,365 | 9 | 540 |
| TOTAL | 3,102 | \$723,009 | 3,016 | \$739,480 | 3,047 | \$791,548 | 3,310 | \$873,857 | 3,337 | \$916,310 | 3,405 | \$934,524 |

RO1 Research Project (Traditional)

To support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing his/her specified interest and competencies.

PO1 Research Program Projects

For the support of a broadly based, multidisciplinary, often long-term research program which has a specific major objective or a basic theme. A program project is directed toward a range of problems having a central research focus in contrast to the usually narrower thrust of the traditional research project.

R35 Outstanding Investigator Grants

To provide long-term support to an experienced investigator with an outstanding record of research productivity. This support is intended to encourage investigators to embark on long-term projects of unusual potential in a categorical program area.

R37 Method to Extend Research in Time (MERIT) Award

To provide long-term grant support to investigators whose research competence and productivity are distinctly superior and who are highly likely to continue to perform in an outstanding manner. Investigators may not apply for a MERIT award. Program staff and/or members of the cognizant National Advisory Council/Board will identify candidates for the MERIT award during the course of review of competing research grant applications prepared and submitted in accordance with regular PHS requirements.

UO1 Research Project (Cooperative Agreement)

To support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing his/her specific interest and competencies.

R29 First Independent Research Support and Transition (FIRST) Award

To provide a sufficient initial period of research support for newly independent biomedical investigators to develop their research capabilities and demonstrate the merit of their research ideas.

RFA Request for Applications

A formal statement which invites grant or cooperative agreement applications in a well-defined scientific area to accomplish specific program purposes and indicates the amount of funds set aside for the competition and/or the estimated number of awards to be made.

R43 Small Business Innovative Research (SBIR) Grants - Phase I

To support projects, limited in time and amount, to establish the technical merit and feasibility of R&D ideas which may ultimately lead to a commercial product(s) or service(s).

R44 Small Business Innovative Research (SBIR) Grants - Phase II

To support in-depth development of R&D ideas whose feasibility has been established in Phase I and which are likely to result in commercial products or services.

R03 Small Grants

To provide research support specifically limited in time and amount for studies in categorical program areas. Small grants provide flexibility for initiating studies, which are generally for preliminary short-term projects and are non-renewable.

R21 Exploratory/Developmental Grants

To encourage the development of new research activities in categorical program areas. Support generally is restricted in level of support and in time.

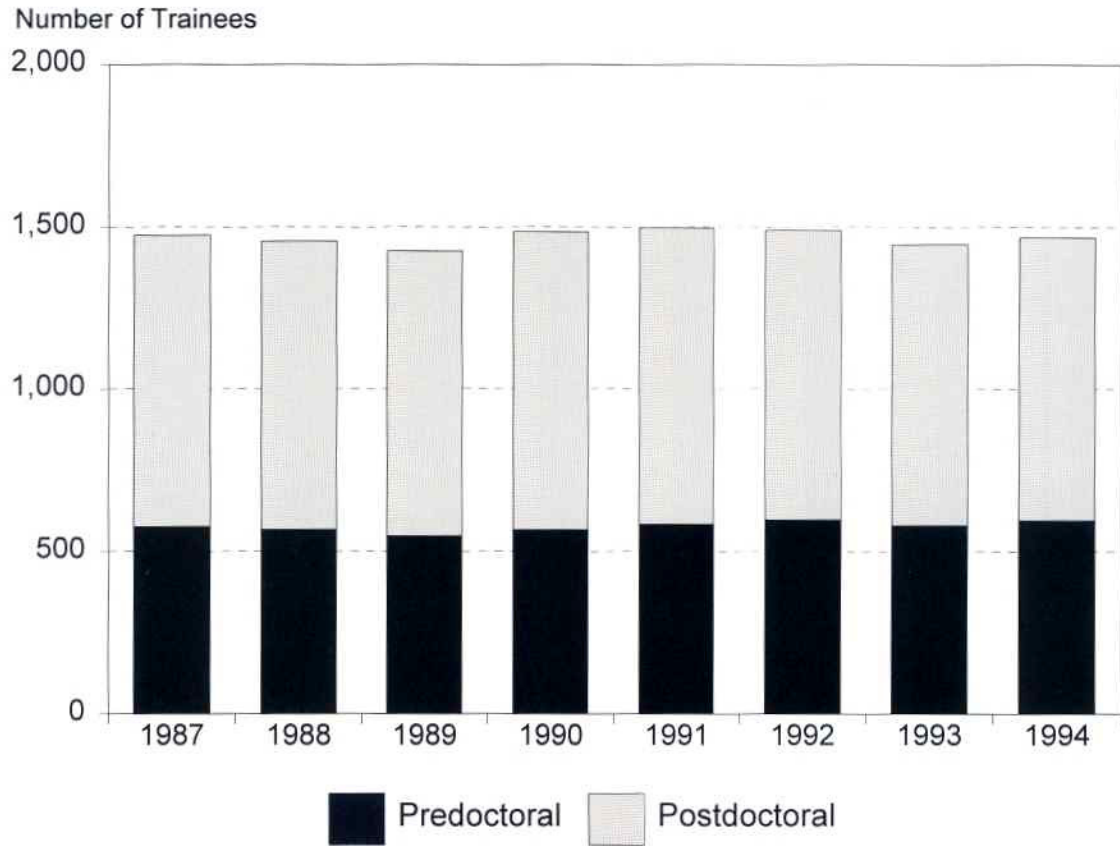
R23 New Investigator Research Awards

To support basic and clinical studies so that newly trained investigators remain active during the development stage of their careers.

R55 Shannon Awards

To provide discrete limited support to scientists whose research applications fall short of the cutoff for funding yet are at the "margin of excellence" whereby the perceived quality of the grant is statistically indistinguishable from grants that are funded.

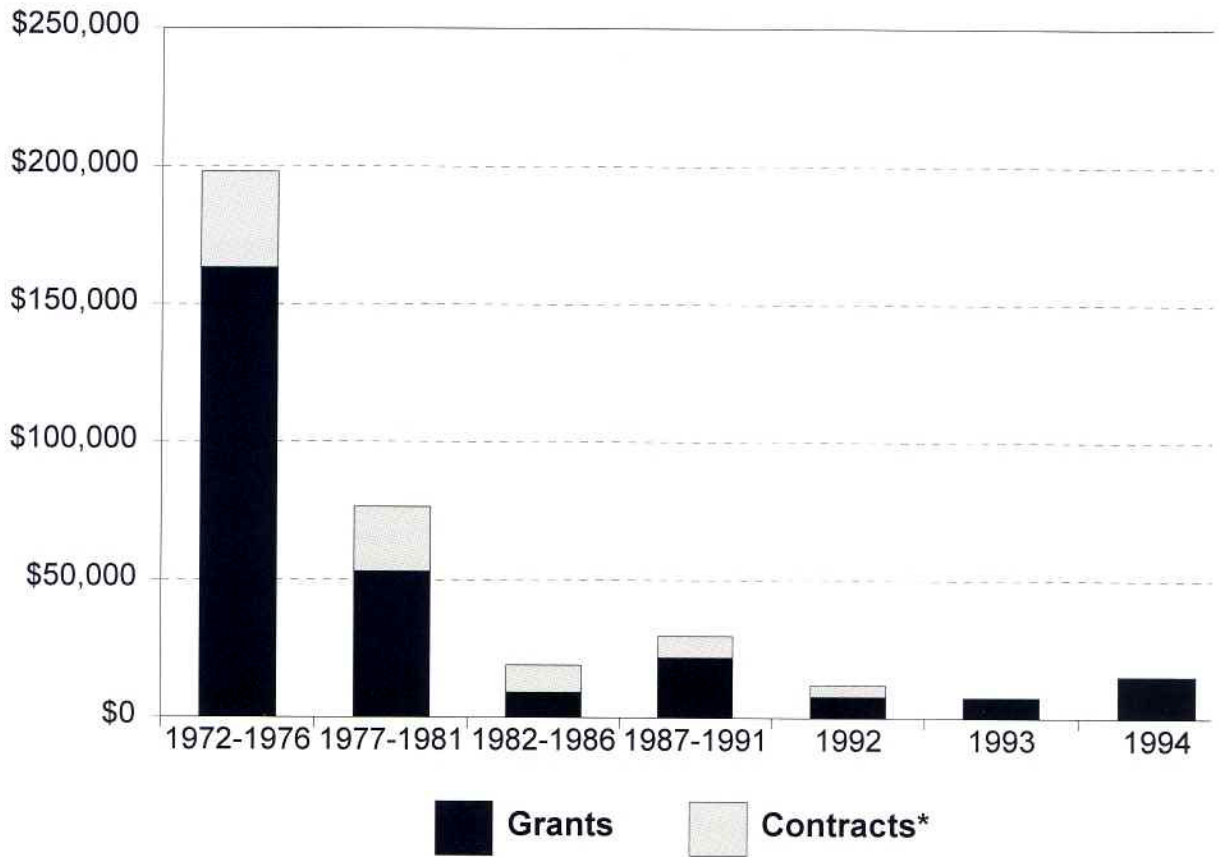
**National Research
Service Awards
Fiscal Years 1987-1994**



| TYPE | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 |
|--------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Predoctoral | 577 | 568 | 548 | 567 | 584 | 597 | 578 | 596 |
| Postdoctoral | 898 | 888 | 880 | 918 | 913 | 894 | 868 | 873 |
| Total | 1,475 | 1,456 | 1,428 | 1,485 | 1,497 | 1,491 | 1,446 | 1,469 |

**Construction/
Renovation Funding
Fiscal Years 1972-1994**

(Dollars in Thousands)



| TYPE | 1972-1976 | 1977-1981 | 1982-1986 | 1987-1991 | 1992 | 1993 | 1994 |
|------------|-----------|-----------|-----------|-----------|---------|---------|----------|
| Grants | \$163,433 | \$53,293 | \$9,225 | \$22,068 | \$8,000 | \$7,182 | \$15,447 |
| Contracts* | 34,644 | 23,232 | 10,093 | 7,935 | 4,000 | 346 | 1,052 |
| Total | 198,077 | 76,525 | 19,318 | 30,003 | 12,000 | 7,528 | 16,499 |

NOTE: Fiscal year 1990 includes \$10 million which was transferred to NCI from other NIH Institutes to partially fund several grants responding to an NIH Construction RFA.
*Includes repair and maintenance at the Frederick Cancer Research and Development Center.

Selected Minority Focused Activities Fiscal Year 1994

- Objectives:**
- Reduce cancer incidence, morbidity and mortality in minority populations by increasing their involvement in the planning and implementation of intervention programs.
 - Increase the number of minority patients involved in NCI-supported clinical trials in order to improve survival and cure rates in these populations.
 - Enhance the intervention capabilities of minority researchers and influence them to develop careers as cancer investigators.
 - Heighten awareness about cancer risk and prevention.
 - Pursue basic research intended to understand the etiology and biology of cancer in defined minority populations.

Strategy: The National Cancer Institute (NCI) has developed mechanisms to broaden participation by minority institutes and individuals in cancer-related research and training activities. NCI seeks to enhance the effectiveness of cancer treatment and control programs in reaching the minority community and other historically underserved segments of the general population.

Minority Activities: **Minority Accrual to Clinical Trials:** A number of factors are potential barriers to minorities participating in clinical trials. Economic and geographic constraints, foreign language barriers, cultural reluctance to seek early medical attention and/or experimental therapy for cancer, and possible physiologic differences, may explain why racial and ethnic minority patients tend to survive for a shorter time after cancer diagnosis than the national average. As part of a multi-faceted NCI plan to improve access to minority participation at all levels of cancer research, the Cancer Therapy Evaluation Program coordinates interrelated clinical programs. The individuals intended to benefit from these programs are Americans of African-American ancestry, Hispanics of Mexican, Puerto Rican, Cuban, or Central American descent, Asian-Americans, and Native Americans, including Alaskans and Hawaiian natives. Eight Cooperative Groups (NSABP, GOG, CCSG, NCCTG, SWOG, RTOG, CALGB, and ECOG) have developed plans to encourage early diagnosis and clinical trials participation among potential patients and to overcome language and logistic barriers for specific minority groups. The NCI has an internal committee to address increasing minority accruals to clinical trials.

Special Populations Studies:

For special populations who experience high cancer rates and are underserved in terms of cancer prevention and control programs, NCI supports initiatives which focus research on interventions designed to address such barriers as cultural and behavioral nuances unique to special population groups as well as obstacles within the health care delivery systems. A study of the impact of socioeconomic status on cancer risk and survival promises to provide information on more effective delivery of cancer intervention programs. In addition, a cancer mapping program will assist local health officials to better target cancer services to such populations. Special populations research also investigates primary prevention interventions designed to meet the specific needs of these groups. Support for several cancer control networks has allowed channeling of cancer prevention and

control information to stimulate interest from culturally sensitive researchers to address the unique needs of special populations.

Etiologic studies are aimed at identifying factors that place specific minority groups at unusual risk for cancer. For example, a series of population-based case-control studies is evaluating possible reasons for African-Americans having higher rates than Caucasians for multiple myeloma and cancers of the pancreas, esophagus and prostate, and to estimate the extent to which race-specific factors may explain these differences. A major prospective study has been launched to evaluate cancer and other health outcomes among farmers and their families, and will include a study site in North Carolina with a large African-American population. Another project is being designed to develop resources for evaluating cancer risks among migrant and seasonal farm workers, with special efforts to include Hispanic and other underserved groups. Studies are also underway to clarify risk factors responsible for the high rates of lung, stomach, oral and cervical cancers among specific minority populations.

Minority Statistics:

NCI's Surveillance Program continues to expand and refine the data collection and analyses of minority populations. Efforts to increase population coverage of Hispanics continued in 1993 and similar efforts are being undertaken for other racial and ethnic groups, low-income populations and the elderly. Expansion of the Program in FY 1992 increased coverage to approximately 14 percent of the total U.S. population. The two new areas included, Los Angeles County and four counties in the San Jose-Monterey area south of San Francisco. The population of Hispanics in these two areas is nearly four million which brings SEER coverage to 22 percent of the total Hispanic population residing in the U.S. This expansion increased coverage of minority populations, notably Asian and Pacific Islanders and African Americans. In addition, 3,400 patients are being followed for survival in the Black/White Survival Study, which was designed to investigate the significance of social, behavioral, lifestyle, biological, treatment, and health care factors as contributors to the observed differences in survival among Black and white cancer cases. Also underway are efforts to describe the cancer incidence and mortality in Alaskan Natives and American Indians as well as the patterns of care, risk factors, and cultural entities that form barriers to early detection and treatment of cancer in these groups.

Minority-Based Community Clinical Oncology Program (MBCCOP):

Supports the development and implementation of effective cancer control and treatment strategies in minority populations by including these groups in clinical trials research as well as provides minority cancer patients with access to state-of-the-art cancer treatment and technology. MBCCOPs are located in seven states and Puerto Rico and are funded through 1994 involving over 275 physicians. Nearly 1,000 patients have been enrolled onto cancer prevention, control, and treatment clinical trials through this program.

Through this effort NCI aims to meet an important need of cancer patients and individuals at risk by establishing a system of oncology programs for participation in clinical research trials through the NCI networks.

Minority Health Professional Training Initiative (MHPTI):

Initiated in 1991, the MHPTI is supporting training and career development opportunities for minority health professionals by engaging them in cancer research or by providing them with training in subspecialties related to cancer.

Such opportunities will increase the number of minority clinicians, clinical researchers, and other health professionals who are prepared to deal with the problem of excess mortality among minority populations due to cancer. As the result of three Requests for Applications (RFAs) published in 1992, four awards to minority clinicians were made. The program has continued through program announcements and two additional awards which were approved for funding in 1993.

Awards are made through the K07, K08, and K14 mechanisms, with an R25 under development. An RFA was issued inviting applications from traditionally historic black colleges and universities. Awards will be issued in FY 95.

Cancer Communications:

To promote clinical trials to minority and low literate target audiences, special training will be designed for NCI staff, educational resources for patient audiences will be developed, and training programs and resources will be designed for health professionals. Preliminary work has begun on the development of easy-to-read consent forms and this work will be expanded. Future efforts will involve continued work with the clinical trials cooperative groups in efforts to address the recruitment of minority patients.

The Cancer Information Service (CIS) awarded 19 new five year contracts which assure regional CIS services will be provided to the entire US population. The CIS Outreach Coordinators work with NCI-designated programs to tailor NCI messages and initiatives to local populations, with a special focus on minority populations. As part of CIS's outreach function, regional offices develop relationships with programs at the regional and state levels to promote knowledge of cancer control and education activities and to provide technical support and materials within the service area. Many designated programs are specifically concerned with minority health including: CCOPs (including the Minority CCOPS), NBLIC, ALIC and NHLIC, CDC Breast and Cervical Cancer Screening Grantees, and State Health Departments. In addition, it is the role of the CIS Outreach Coordinators to act as advocates for minority and low literate populations when working with Comprehensive and Clinical Cancer Centers, Patient Educators Network, and Data-Based Intervention Research Grantees on regional initiatives. The outreach efforts of the CIS also includes working with minority media and mass media with messages of interest to regional minority populations.

Existing resources for patients and health professionals are continually revised. The special needs of minority populations and low-literate groups are incorporated in the revision of all resources and the development and design of new resources.

The NCI's Comprehensive Minority Biomedical Program (CMBP) continues its efforts to heighten awareness about cancer risk and prevention in African Americans. The aim of this undertaking is to develop and disseminate information through educational programs regarding steps that can be taken to control or reduce cancer in African Americans.

The NCI's CMBP issued an RFA inviting research grant applications from interested investigators with access to large or predominantly minority populations. The Minority Enhancement Awards promote minority group participation in cancer research with a special focus on cancer control research. Support provided by this initiative broadens the operational base of each institution by: expanding cancer control and prevention efforts in early detection, prevention screening, pre-

treatment evaluation treatment, continuation care, and rehabilitation; increasing the involvement of minority population primary care providers early in the course of clinical treatment research; promoting the involvement in treatment research at the institutional level with a focus on the development of treatment protocols for cancers that have a high incidence in minorities; supporting programs involving diet and nutrition cancer control activities.

NCI continued to expand its African American Cancer Education program -- "Do the right thing...Get a new attitude about cancer." "Do the right thing" urges African Americans to adopt a "new attitude" and make some simple lifestyle changes as crucial steps toward maintaining good health.

NCI also continued distribution and promotion of the Hispanic Program Kit "Hagalo hoy...Por su salud y su familia," which focused on early detection of breast and cervical cancers. The kit, developed for community leaders and organizations serving the Hispanic population, serves as a resource for community leaders to develop cancer education programs, particularly for breast and cervical cancer. The kit contains education materials such as brochures and factsheets that can be used for community events such as fairs, workshops, meetings and conferences. It also contains articles and camera-ready graphics to be used for local media placements. Short and simple breast and cervical cancer bilingual brochures were printed in large quantities for mass distribution.

Project Awareness is a collaborative program designed to provide underserved women with breast cancer education, mammography, clinical breast exams, and followup medical care. It was completed in 10 cities including: Washington, D.C.; Detroit, Michigan; Los Angeles, California; Baltimore, Maryland; Atlanta, Georgia; Raleigh/Durham, North Carolina; St. Louis, Missouri; and Miami, Florida. Evaluation data on the effectiveness of the education campaign is now being completed. A revised program manual has been produced and will be available to interested cities. The community-based model is now being used by the YWCA in cooperation with the CDC to institutionalize the program. The Cancer Information Service (CIS) and National Black Leadership Initiative on Cancer (NBLIC) will "co-chair" local efforts providing media relations and technical support as needed.

NCI continued distribution and promotion of the half-hour television special and public service announcements on mammography "Una Vez al ano...Para toda una vida." The TV special was developed as a tool for educating Hispanic women on the need for breast cancer screening. "Una vez..." aired on the Univision Spanish-language television network for the second time during Breast Cancer Awareness Month in October 1993. Over 8,000 copies have been distributed to organizations serving the Hispanic population in the United States and Puerto Rico. The film is also being used widely by the Centers for Disease Control and Prevention Breast and Cervical Cancer Grantees, State Health Departments, the Puerto Rico Department of Health, and by many units of the American Cancer Society.

The NCI produced a 9-minute video entitled, "Taking Control of Your Health: The Pap Test and Cervical Cancer." This video is the first culturally-appropriate, intertribal video on cervical cancer for Native American women. Clear, simple language is used to give an overview of the cervical cancer problem among Native American women (many times more prevalent than in the population at large), an explanation of the Pap test, recommendations for screening, and ways that women may be able to protect themselves from the disease. Women of all ages are addressed in the video, from sexually active teens to women past menopause. The film was premiered at a national meeting of Native American women. The film

in conjunction with its original musical score and support materials will be distributed through Native American intermediaries.

Several basic print brochures on cervical cancer were developed and tested for special audiences including low literate, African American and Hispanic women.

A tipsheet on how to quit smoking for African Americans and a bilingual piece for Hispanics were developed and widely disseminated during National Minority Cancer Awareness Month and throughout the year.

NCI collaborated in the revision and update of the "Guia para dejar de fumar," a smoking cessation guide developed by the University of San Francisco Network on Hispanic/Latino Tobacco Control Program. The Guia will be printed by the NCI and be part of the Hispanic Education Program resources.

NCI developed and tested nutrition education materials for low literacy segments of specific ethnic populations. These populations include American Indians, Alaskan Natives, Hawaiian Natives, Chinese, Filipino, Vietnamese, Hispanics, African Americans, and Caucasians. A total of 43 pieces have been developed which include tipsheets, booklets, posters, and scripts for three video and one audio tape. Some of these materials are bilingual and are currently being pretested with appropriate groups across the country. A guide for physicians, "Teaching Your Ethnic Patients," is also being developed. These materials will be available in the Fall of 1994.

The "**Down Home Healthy Cookbook**" was developed by NCI in conjunction with two nationally known African American chefs. They worked with the NCI by taking recipes that are popular among African Americans and making them lower in fat and sodium. This cookbook is being used by numerous African American organizations in their nutrition education programs. The regional CIS offices have been working with local intermediaries for distribution of the booklet.

Appropriations of the NCI 1938-1994

| | | | |
|---|-------------------------|-----------------------|----|
| 14.0% \$4,410,425,220 | 1938 through 1968..... | \$1,690,550,220 | |
| | 1969..... | 185,149,500 | |
| | 1970..... | 190,486,000 | |
| | 1971..... | 230,383,000 | |
| | 1972..... | 378,794,000 | |
| | 1973..... | 492,205,000 | |
| | 1974..... | 551,191,500 | |
| | 1975..... | 691,666,000 | 1 |
| 86.0% \$27,142,476,000 | 1976..... | 761,727,000 | |
| | "TQ"..... | 152,901,000 | 2 |
| | 1977..... | 815,000,000 | |
| | 1978..... | 872,388,000 | 3 |
| | 1979..... | 937,129,000 | |
| | 1980..... | 1,000,000,000 | 4 |
| | 1981..... | 989,355,000 | 5 |
| | 1982..... | 986,617,000 | 6 |
| | 1983..... | 987,642,000 | 7 |
| | 1984..... | 1,081,581,000 | 8 |
| | 1985..... | 1,183,806,000 | |
| | 1986..... | 1,264,159,000 | 9 |
| | 1987..... | 1,402,837,000 | 10 |
| | 1988..... | 1,469,327,000 | 11 |
| | 1989..... | 1,593,536,000 | 12 |
| | 1990..... | 1,664,000,000 | 13 |
| | 1991..... | 1,766,324,000 | 14 |
| 1992..... | 1,989,278,000 | 15 | |
| 1993..... | 2,007,483,000 | 16 | |
| 1994..... | 2,082,267,000 | | |
| 1995..... | 2,135,119,000 | 17 | |
| | Total | | |
| | (1938-1995)..... | 31,552,901,220 | |

Transition Quarter ("TQ") --

July 1, 1976 through September 30, 1976. The interim period in changing of the Federal Fiscal Year from July 1 through June 30 to October 1 through September 30.

- ¹ Includes \$18,163,000 for training funds provided by Continuing Resolution.
- ² Includes \$3,201,000 for training funds provided by Continuing Resolution.
- ³ Includes \$20,129,000 for training funds provided by Continuing Resolution.
- ⁴ 1990 appropriation authorized under a Continuing Resolution.
- ⁵ Reflects 1981 rescission of \$11,975,000.
- ⁶ Amount included in continuing resolution. Includes \$47,988,000 transferred to the National Institute of Environmental Health Sciences for the National Toxicology Program.
- ⁷ Appropriated under Continuing Resolution and Supplemental Appropriation Bill.
- ⁸ Includes \$23,861,000 for training funds provided by a Continuing Resolution and \$4,278,000 in a Supplemental Appropriation Bill.
- ⁹ Includes \$6,000,000 from a Supplemental Appropriation Bill.
- ¹⁰ Authorized under Omnibus Continuing Resolution.
- ¹¹ Authorized under Omnibus Continuing Resolution.
- ¹² Appropriation prior to reduction contained in G.P. 517 (-\$19,122,000) and G.P. 215 (-\$2,535,000) and P.L. 100-436, Section 213, (-\$1,013,000).
- ¹³ Appropriation prior to reduction contained in P.L. 101-166 (-\$6,839,000) and P.L. 101-239 (-\$22,829,000).
- ¹⁴ Appropriation prior to reductions in P.L. 101-517 (-\$8,972,000 for salary and expense reduction; -\$42,568,000 for across-the-board reduction).
- ¹⁵ Appropriation prior to reductions in P.L. 102-170 (-\$21,475,000 for salary and expense reduction; -\$1,262,000 for travel reduction; \$15,000,000 transferred to other institutes for cancer research).
- ¹⁶ Appropriation prior to reductions in P.L. 102-294 (-\$16,060,000 for .8% reduction to all line items; -\$9,933,000 for S&E reduction; -\$139,000 for consultant services reduction).
- ¹⁷ Appropriation prior to reductions in PL 103-211 (-\$1,883,000 for Procurement Reduction; -\$116,000 for SLUC Reduction; -\$1,052,000 for Bonus Pay Reduction). Includes \$218,199,000 of AIDS funding.

**By-Pass Budget
Requests
Fiscal Years 1973-1996**

| Fiscal Year | Request |
|------------------------|----------------|
| 1973..... | \$550,790,000 |
| 1974..... | 640,031,000 |
| 1975..... | 750,000,000 |
| 1976..... | 898,500,000 |
| 1977..... | 948,000,000 |
| 1978..... | 955,000,000 |
| 1979..... | 1,036,000,000 |
| 1980..... | 1,055,000,000 |
| 1981..... | 1,170,000,000 |
| 1982..... | 1,192,000,000 |
| 1983..... | 1,197,000,000 |
| 1984..... | 1,074,000,000 |
| 1985..... | 1,189,000,000 |
| 1986..... | 1,460,000,000 |
| 1987..... | 1,570,000,000 |
| 1988..... | 1,700,000,000 |
| 1989..... | 2,080,000,000 |
| 1990..... | 2,195,000,000 |
| 1991..... | 2,410,000,000 |
| 1992..... | 2,612,000,000 |
| 1993..... | 2,775,000,000 |
| 1994..... | 3,200,000,000 |
| 1995..... | 3,600,000,000 |
| 1996..... | 3,640,000,000 |

NOTE: Following the original passage of the National Cancer Act in December, 1971, a provision was included for the Director of the National Cancer Institute to submit a budget request directly to the President; hence it has come to be called the Bypass Budget. The Budget submitted for 1973 was the initial submission.

**Comparison of Dollars,
Positions and Space
Fiscal Years 1972-1994**

| | Dollars | | Positions | | Space** | |
|-------------|-----------------------|-------------------------------------|--------------------------------------|-------------------------------------|-------------------------------|-------------------------------------|
| | Obligations (\$000's) | Percent of Increase Over Prior Year | Actual Full-Time Permanent Employees | Percent of Increase Over Prior Year | Allocated Space (Square Feet) | Percent of Increase Over Prior Year |
| 1974 | 581,149 | | 1,805 | | 381,436 | |
| 1975 | 699,320 | 20.3% | 1,849 | 2.4% | 382,485 | 0.3% |
| 1976 | 760,751 | 8.8% | 1,955 | 5.7% | 387,324 | 1.3% |
| 1977 | 814,957 | 7.1% | 1,986 | 1.6% | 428,285 | 10.6% |
| 1978 | 872,369 | 7.0% | 1,969 | -0.9% | 491,725 | 14.8% |
| 1979 | 936,969 | 7.4% | 1,973 | 0.2% | 493,156 | 0.3% |
| 1980 | 998,047 | 6.5% | 1,837 | -6.9% | 467,730 | -5.2% |
| 1981 | 989,338 | -0.9% | 1,815 | -1.2% | 472,633 | 1.0% |
| 1982 | 986,564 | -0.3% | 1,703 | -6.2% | 477,782 | 1.1% |
| 1983 | 986,811 | 0.0% | 1,731 | 1.6% | 484,093 | 1.3% |
| 1984 | 1,081,460 | 9.6% | 1,698 | -1.9% | 466,890 | -3.6% |
| 1985 | 1,177,853 | 8.9% | 1,596 | -6.0% | 466,890 | 0.0% |
| 1986 | 1,210,284 | 2.8% | 1,573 | -1.4% | 465,790 | -0.2% |
| 1987 | 1,402,790 | 15.9% | 1,642 | 4.4% | 465,790 | 0.0% |
| 1988 | 1,468,435 | 4.7% | 1,708 | 4.0% | 458,556 | -1.6% |
| 1989 | 1,570,342 | 6.9% | 1,701 | -0.4% | 483,778 | 5.5% |
| 1990 | 1,644,330 * | 4.7% | 1,837 | 8.0% | 489,604 | 1.2% |
| 1991 | 1,712,669 | 4.2% | 1,921 | 4.6% | 499,396 | 2.0% |
| 1992 | 1,947,571 | 13.7% | 2,042 *** | 6.3% | 477,067 | -4.5% |
| 1993 | 1,978,340 | 15.5% | 1,951 *** | -4.5% | 493,186 | 3.4% |
| 1994 | 2,076,218 | 6.6% | 1,840 *** | -5.7% | 472,545 | -4.2% |

* Includes \$10,130 which was transferred to NCI from other NIH Institutes to partially fund several grants responding to a NIH Construction RFA.

** Does not include space at the Frederick Cancer Research and Development Center.

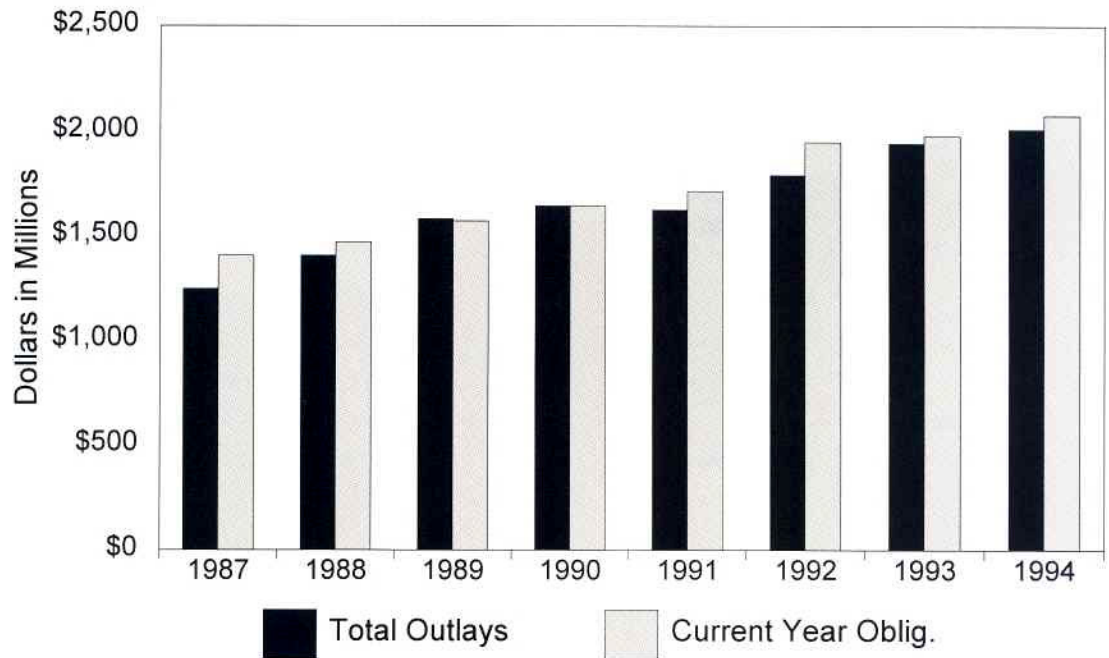
*** Source NIH TDCS 866

**Personnel
Resources
Fiscal Years
1985-1994**

| Fiscal Year | --Number of Full Time Equivalents-- | | | Number of Employees |
|-------------|-------------------------------------|------|-------|---------------------|
| | Cancer | AIDS | Total | |
| 1985 | 2,145 | 85 | 2,230 | 2,195 |
| 1986 | 2,003 | 98 | 2,101 | 2,096 |
| 1987 | 1,981 | 129 | 2,110 | 2,272 |
| 1988 | 2,137 | 146 | 2,283 | 2,302 |
| 1989 | 1,985 | 188 | 2,173 | 2,201 |
| 1990 | 1,960 | 232 | 2,192 | 2,322 |
| 1991 | 2,045 | 300 | 2,345 | 2,437 |
| 1992 | 2,219 | 306 | 2,525 | 2,604 |
| 1993 | 2,184 | 300 | 2,484 | 2,425 |
| 1994 | 2,081 | 301 | 2,382 | 2,307 |

**National Cancer Institute
Obligations and Outlays
Fiscal Year 1987-1994**

(Dollars in Millions)



| \$ in Millions | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 |
|--------------------------|---------|---------|---------|---------|---------|---------|---------|---------|
| Prior Year Outlays | \$680 | \$723 | \$815 | \$885 | \$885 | \$831 | \$1,099 | \$1,108 |
| Current Year Outlays | 565 | 680 | 765 | 759 | 739 | 961 | 843 | 901 |
| Total Outlays | 1,245 | 1,403 | 1,580 | 1,644 | 1,624 | 1,792 | 1,942 | 2,009 |
| Current Year Obligations | \$1,403 | \$1,468 | \$1,570 | \$1,644 | \$1,713 | \$1,948 | \$1,978 | \$2,076 |

Obligations: Orders placed, grants awarded, contract increments funded, salaries earned and similar financial transactions which legally utilize or reserve an appropriation for expenditure.

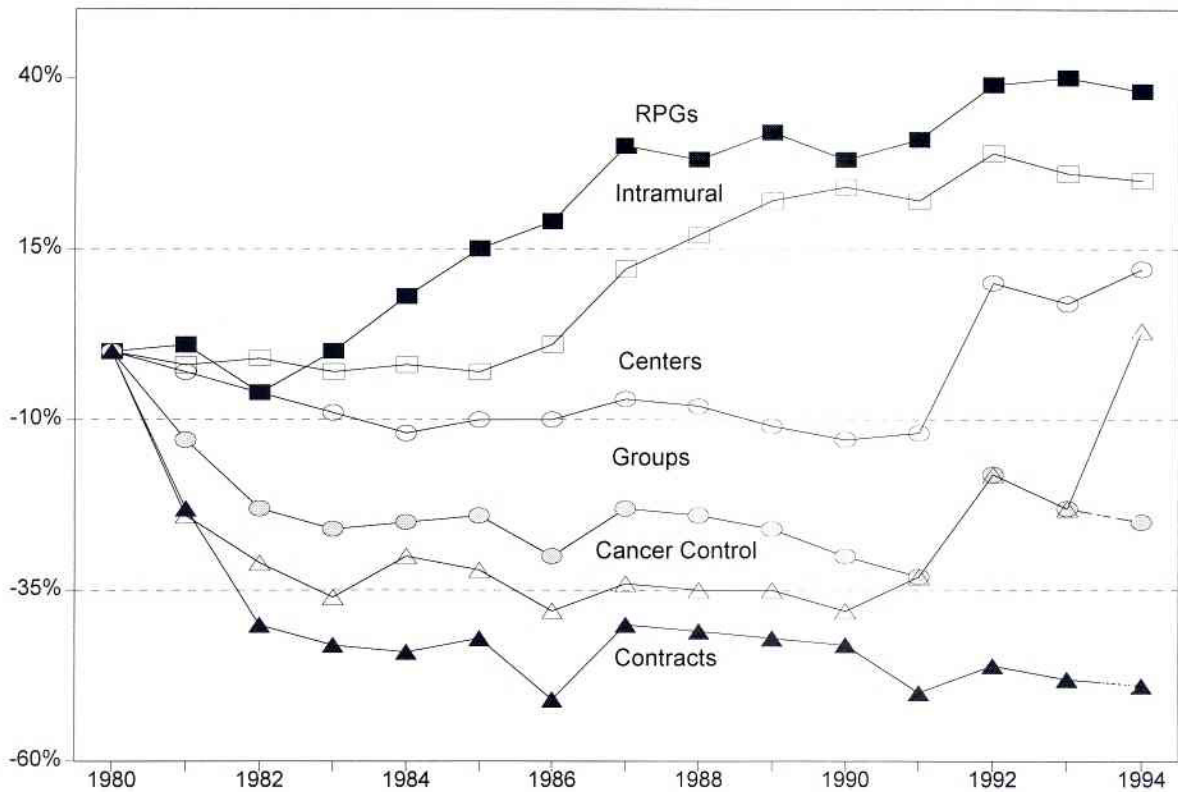
Outlays: Payments (cash or checks) made from appropriations.

Constant Dollar Trends

(Dollars in Millions)

Fiscal Years 1980-1994

Percent Change in Obligations as 1980 Constant Dollars



| Constant Dollars: | 1980 | 1982 | 1984 | 1986 | 1988 | 1990 | 1992 | 1994 |
|-----------------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Research Project Grants | \$321 | \$300 | \$346 | \$382 | \$412 | \$412 | \$445 | \$443 |
| Cancer Prevention & Control | 67 | 46 | 47 | 42 | 43 | 42 | 55 | 69 |
| Centers & SPOREs | 67 | 63 | 59 | 60 | 62 | 59 | 74 | 75 |
| Intramural Research | 142 | 141 | 139 | 143 | 166 | 177 | 183 | 178 |
| Clinical Cooperative Groups | 48 | 37 | 36 | 34 | 37 | 33 | 39 | 36 |
| R&D Contracts | 189 | 114 | 106 | 92 | 111 | 107 | 102 | 97 |
| Subtotal | 834 | 701 | 734 | 753 | 831 | 829 | 898 | 897 |
| All other mechanisms | 124 | 90 | 77 | 75 | 77 | 81 | 93 | 86 |
| Total NCI | \$958 | \$791 | \$811 | \$827 | \$908 | \$910 | \$991 | \$983 |
| NCI Change over 1980 | base | -17% | -15% | -14% | -5% | -5% | 3% | 3% |

| Current Dollars: | 1980 | 1982 | 1984 | 1986 | 1988 | 1990 | 1992 | 1994 |
|-----------------------------|-------|-------|---------|---------|---------|---------|---------|-------|
| Research Project Grants | \$321 | \$358 | \$461 | \$559 | \$666 | \$740 | \$874 | \$935 |
| Cancer Prevention & Control | 67 | 55 | 63 | 61 | 70 | 75 | 108 | 145 |
| Centers & SPOREs | 67 | 75 | 79 | 88 | 100 | 105 | 145 | 158 |
| Intramural Research | 142 | 168 | 186 | 209 | 269 | 317 | 360 | 375 |
| Clinical Cooperative Groups | 48 | 44 | 48 | 49 | 59 | 60 | 77 | 76 |
| R&D Contracts | 189 | 136 | 142 | 135 | 180 | 192 | 201 | 205 |
| Subtotal | 834 | 836 | 979 | 1,101 | 1,344 | 1,489 | 1,765 | 1,894 |
| All other mechanisms | 124 | 107 | 103 | 109 | 125 | 145 | 183 | 182 |
| Total NCI | \$958 | \$943 | \$1,082 | \$1,210 | \$1,469 | \$1,634 | \$1,948 | 2,076 |

| Deflators | 1.0 | 1.2 | 1.3 | 1.5 | 1.6 | 1.8 | 2.0 | 2.1 |
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|

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