Catalyst For Cures

How Federally Funded Cancer Research Saves Lives

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Cancer is the leading threat to health in our country. It reaches indiscriminately into every community and touches every family. Much more research is needed to meet the challenges we continue to face with this disease.

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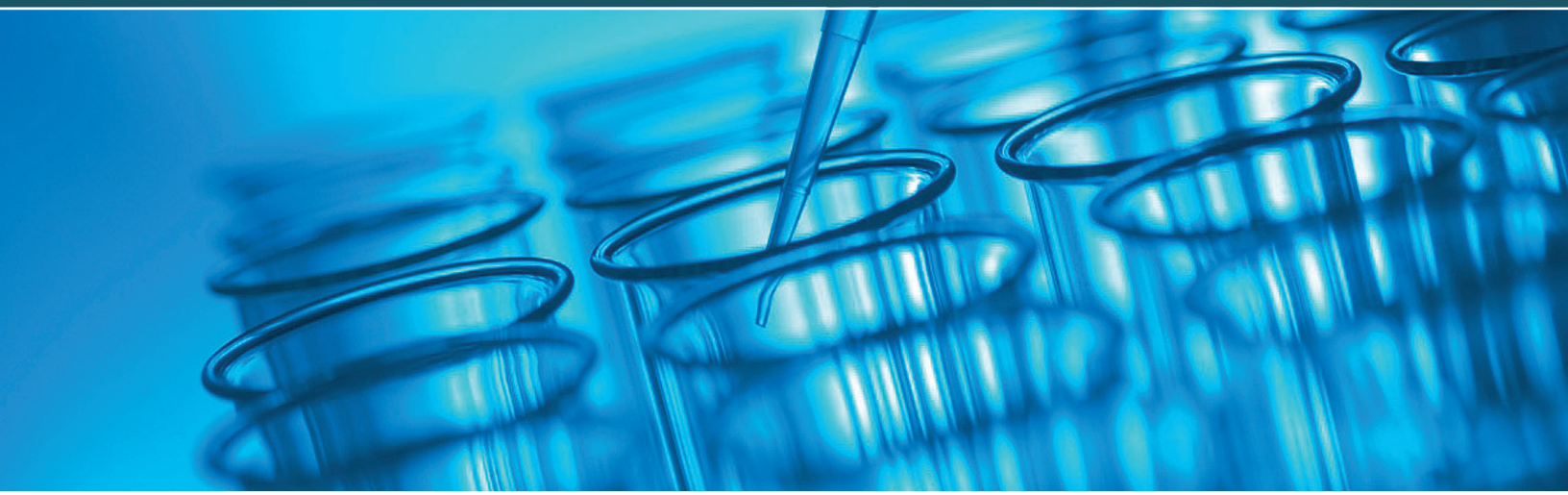


Foreword

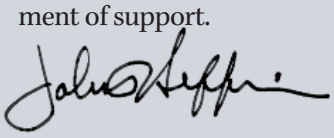
Today, nearly 14 million cancer survivors are alive in the United States thanks to improved screening tools, more effective treatments, and a greater understanding of proven prevention strategies. Research funded by the National Institutes of Health (NIH) and the National Cancer Institute (NCI)—both federal institutions—and conducted at thousands of public and private institutions across the country has led to these advances and a steady decline in cancer death rates since the 1990s.

As the largest private, not-for-profit funder of cancer research in the United States, the American Cancer Society helps young investigators stay in the field as their work moves forward and begins to bear fruit. Many of these investigators go on to compete for and receive NIH support. Some ultimately make the discoveries that lead to breakthroughs against the disease. These include 46 distinguished Nobel laureates who are past Society grantees.

The American Cancer Society has devoted more than $3.8 billion to the effort since its research program began in 1946 and in 2011 invested more than $148 million in research. As impressive as these numbers are, no sustained advancement against cancer would happen without the federal government's robust research effort at the NIH. In 2011, the NIH supported more than $5.4 billion in cancer research. For decades, research funded by the NIH and the NCI has played a role in every major cancer prevention, detection, and treatment advance, while also delivering scientific breakthroughs for many other diseases.

Roughly half of all cancer deaths could be averted by applying the knowledge we've gained so far. Yet much work remains. The Society estimates that, in 2012, more than 1.6 million people in this country were expected to be diagnosed with cancer and more than 570,000 were expected to die from the disease. Cancer costs our nation hundreds of billions of dollars each year in medical care and lost productivity. Moreover, cancer incidence rates are expected to climb dramatically as our population ages.

This report from the American Cancer Society Cancer Action Network, the Society's advocacy affiliate, highlights the role NIH and NCI funding has played in recent advances, the progress the cancer community continues to make, and the promise of continued federally funded cancer research. The researchers and patients profiled here show what can be accomplished through collaboration, broad participation in the research enterprise, and support across all sectors. Their stories also demonstrate that the path to progress is a marathon, not a sprint, and demands a sustained commitment of support.



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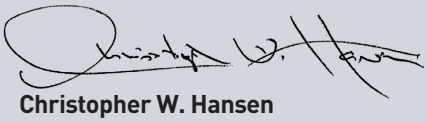

Christopher W. Hansen
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Introduction

A Disease Defined by Questions

How does cancer of the lung spread to the brain? Why do two melanoma treatments provoke no response in a patient, yet the third knocks out the cancer entirely? And what role do proteins, enzymes, and T-cells play in these stories?

The more than 200 conditions known as cancer are among medicine's greatest mysteries. The overarching cause is deceptively simple: cells behaving badly. But why do these cells grow and mutate in abnormal, destructive ways?

Complex questions must be answered before any therapy reaches the marketplace or any patient experiences its benefits. Tracking down answers to these questions is the essential role basic research plays at the beginning of the drug development process.

A Starting Point for Answers

In the history of scientific research, progress has built upon itself one incremental discovery at a time. The medicines we use today, the practices we follow, and the equipment that facilitates progress all exist because of findings in molecular biology, genetics, and other highly specialized sciences.

These findings begin with basic research. Through basic research, cancer investigators focus on what drives the proliferation and survival of cancer cells and develop new treatments based on their discoveries. Clinical trials move basic research forward by testing how well emerging medical approaches work in people. These experimental research studies provide cancer patients with access to new and often improved experimental treatments at a time when conventional treatment options are limited or ineffective.

Basic research also generates the insights that lead to better ways of conducting science and commercializing findings. When sustained over decades, basic research leads to career growth, mentorships, and game-changing ideas.

Discoveries in basic research have made possible the treatments cancer patients worldwide depend on today.

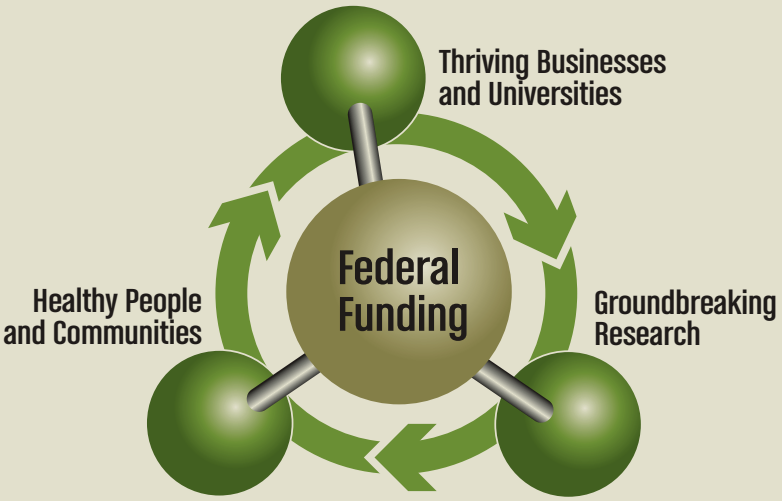
Government's Essential Role

Basic cancer research demands extensive resources, encompasses a timetable that can span decades, and yields outcomes that often are difficult to predict. The journey is frequently too nebulous or costly for a bottom line-driven, private-sector enterprise to take on. The time, equipment, and staffing requirements are too much for even the largest university to shoulder alone. Basic research is an endeavor that demands partnerships—and that's where federal funding comes in.

Since President Richard Nixon signed the National Cancer Act in 1971, universities, medical schools, hospitals, and research

centers supported and funded by the NIH and the NCI have fulfilled the basic research role in the cancer ecosystem. More than $5.4 billion in cancer research grants each year support scientists through their long journeys of discovery.

The NIH offers investigators opportunities that are beyond the ability of academic institutions, such as the chance to conduct basic research and clinical trials in the same project. Nearly every American Nobel Prize-winning scientist has received NIH funding at some point in their careers.



The impact of basic research on individual lives knows no price tag. A lymphoma patient is healthy—and running a marathon—thanks to a therapy whose development began before this individual was born. A pregnant woman diagnosed with breast cancer is able to undergo treatment and successfully carry her pregnancy to term, delivering a healthy baby girl. And new testing controls give researchers nationwide greater precision in their work by improving the consistency of biopsy evaluations.

For more than four decades, the United States has been the world leader in basic cancer research. During this time, research funded by the NIH and the NCI has contributed to our understanding of the most virulent and perplexing cancers, to treatments that have benefited millions of lives, and to an economic engine that generates hundreds of thousands of high-quality jobs and injects tens of billions of dollars into our economy. And this research has laid the foundation for even more life-saving discoveries well into the future.

This report recounts the work of just a few of the thousands of investigators and patients who make such progress possible.

Key Breakthroughs in the Cancer Fight

Disease	Key Findings/Therapies	Interventions
Melanoma	BRAF gene is key cancer indicator, patient's immune system used in the cancer fight	Vemurafenib, Yervoy
Leukemia and lymphoma	Role of signaling networks, potential for molecular targeting and immunotherapy	Gleevec, Rituxan, ABT-199
Lung cancer	Protein behaviors and biomarkers indicate the presence of cancer or the ability to respond favorably to certain therapies.	Gefitinib/Iressa, Taxol, Tarceva
Breast cancer	Therapies for cancers with and without the HER2 receptor	Herceptin, Tigatuzumab
Colorectal cancer	Certain antibodies interfere with cell growth and behavior.	Avastin, Erbitux
Cervical cancer	A vaccine to prevent a virus known to cause cancer	Gardasil

Melanoma

Yervoy—Self-defense in a Stage IV Battle

"I was feeling really down, with little hope," says Ken Stock, a retired lawyer and father of three who had been in good health for most of his life. A routine follow-up visit after the removal of melanoma tumors on his back revealed that his cancer had progressed to stage IV. Doctors told him no further treatments were available.

> "This trial gave me hope. I went from thinking that nothing was available and that I would have to accept my fate to a 180-degree turnaround."
>
> *Ken Stock, stage IV melanoma survivor*

Fortunately, physician and oncologist friends directed Ken to a blog where stage IV melanoma patients shared information about places to receive treatment. Their advice led him to clinical trials run by Dr. Geoffrey Weiss* at the University of Virginia's Human Immune Therapy Center.

Here Ken received high doses of Yervoy, a drug rooted in federally funded research. Yervoy uses T-cells from a patient's own immune system to fight cancer and is an alternative to traditional chemotherapy, which indiscriminately kills healthy cells along with cancer cells and can bring on a host of debilitating side effects.

Even while taking high doses of Yervoy, Ken says he has experienced minimal side effects. Most incredibly, his latest checkup showed no evidence of cancer.

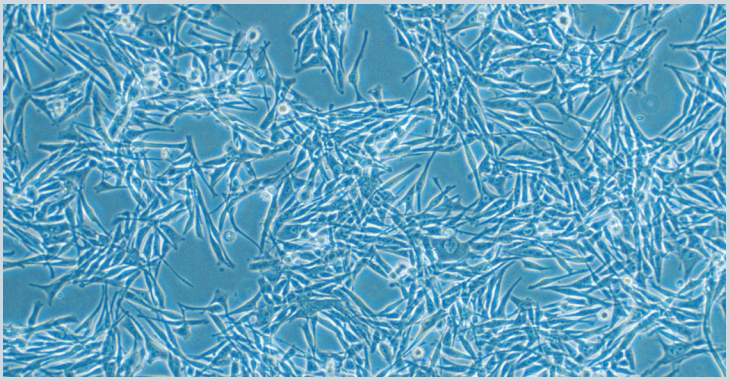
In the lab and through clinical trials with patients like Ken, Dr. Weiss has been on the trail of cancer's causes and cures since 1982. Working in collaboration with researchers at the University of Texas Health Science Center, he contributed to the clinical advance of 40 new anti-cancer agents. And his research with the Cytokine Working Group, an NCI-funded, multi-institutional consortium, led to the development of an FDA-approved therapy for cancers including malignant melanoma.

Today, Dr. Weiss and his colleagues at the University of Virginia are making even more discoveries and connecting roughly 40 melanoma patients a year to new therapies with expanded treatment options for a disease that used to be considered a death sentence.

Clinical trials conducted by Dr. Weiss' team test therapies that train a patient's immune system to turn against cancer by targeting the molecules that cause tumor growth and progression. It is work that federal funding for cancer research makes possible. NCI grants totaling approximately $5 million have helped support Dr. Weiss, his laboratory, and his clinical trials. In addition, some of the trials are administered through the NCI-funded, public-private Eastern Cooperative Oncology Group, one of the largest coordinators of cancer clinical trials in the United States.

* Has received American Cancer Society funding

Milestones in the Melanoma Fight



How do initial observations of cell behavior lead to the production of major cancer-fighting drugs? In many cases, research funded by the NIH and the NCI generates the incremental discoveries that spur progress.

The timeline here outlines the creation of two drugs—Zelboraf, which targets melanoma in patients who have a mutation in the BRAF gene, and Yervoy, a long-sought option for patients with advanced-stage melanoma. Before the late 1990s, the few treatment options available for advanced melanoma either brought on severe side effects or worked for only a small number of patients.

Mid-1990s Discovery of the CTLA-4 protein lays the foundation for Yervoy's development: Dr. James Allison* at the University of California, Berkeley, discovered a specific protein, CTLA-4, that prevents T-cells from fighting melanoma and other illnesses—an initial step in the development of Yervoy.

1998 The pharmaceutical industry moves Yervoy's creation forward: Private-sector development of an antibody that blocks the cancer-causing CTLA-4 protein marked an important milestone in Yervoy's development.

2002 Establishment of the BRAF gene/cancer link kicks off Zelboraf's development: Two-thirds of all human melanoma cells carry the BRAF gene. Among these, 80 percent share a single mutation. The large international group of researchers behind this finding included Dr. Gregory Riggins, from the Johns Hopkins Center for Global Health, whose work had been funded by NCI grants since 2000, and Dr. Barbara Weber, from the Abramson Cancer Center/University of Pennsylvania School of Medicine, whose work was funded by NCI grants from 1990 to 2005.

* Has received American Cancer Society funding

Melanoma

Milestones in the Melanoma Fight

2002–2010 Research moves Zelboraf closer to market: NCI-supported laboratory studies at five institutions helped identify the genetic cause behind melanoma drug resistance. Subsequent research showed that the compound that eventually became Zelboraf halted the growth of—and even shrank—BRAF-associated tumors in mice and generated a positive response in humans. This research was partially funded by an NCI grant to Dr. Katherine L. Nathanson, at the University of Pennsylvania, whose work has been consistently funded by NCI grants since 2000.

2003 Yervoy shows promise against advanced-stage cancer: Two NCI-funded clinical trials revealed this drug's ability to unleash cancer-killing T-cells in patients with late-stage melanoma, as well as in patients with ovarian cancer.

2010 For Zelboraf, side effects spur further investigation: Many melanoma patients treated with the compound that ultimately became Zelboraf were developing another type of skin cancer. Dr. Kevan Shokat at the University of California, San Francisco, and Dr. Neal Rosen*, at Memorial Sloan-Kettering Cancer Center, discovered the cause: the drug was interfering with other signals in the cancer cell. This breakthrough—crucial to moving Zelboraf closer to market—was partially funded by an NCI grant to Dr. Rosen, whose work has been consistently supported by NCI grants since 1989.

2011 Zelboraf approved for patients with BRAF gene: After clinical trials showed a higher survival rate (84 percent vs. 64 percent) and slower cancer progression in patients treated with Zelboraf, the FDA approved it for treating melanoma patients with the BRAF gene.

2011 Yervoy approved for advanced melanoma patients: Yervoy became the first therapy that extended overall survival for advanced melanoma patients. Researchers also believe it holds promise for treating prostate, lung, and other cancers.

* Has received American Cancer Society funding

The Third Trial's the Charm

For 30 years, Dr. Marc Ernstoff* has been researching and developing new therapies for cancer, including the most advanced forms of malignant melanoma. Like Dr. Weiss, he has been involved with the Cytokine Working Group. Today, supported by NIH and NCI grants, Dr. Ernstoff conducts research, runs a lab, and manages clinical trials at the Dartmouth-Hitchcock Norris Cotton Cancer Center.

By expanding treatment options in the fight against melanoma, his team's work gives patients like Carolyn Sumner new hope.

A busy mother of four and a training manager for a large international company, Carolyn was initially diagnosed with melanoma in 1994. Before realizing how advanced the melanoma had become, she went through the standard therapy at the time: a series of chemotherapy treatments. Chemotherapy, which uses powerful chemicals to kill cancer cells, is often accompanied by harsh side effects. Even so, shortly after she finished chemotherapy, the cancer returned and spread swiftly throughout her body.

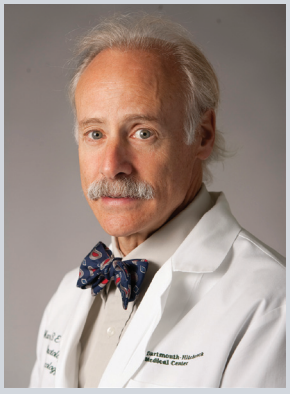
Due to the advanced nature of Carolyn's melanoma, a clinical trial was her only hope. In an effort to try to save her life, she played an important role in advancing the scientific march against her disease.

At the Dartmouth-Hitchcock Norris Cotton Cancer Center, Carolyn met Dr. Ernstoff, who became her oncologist and advocate. In two different clinical trials, she received treatments that harnessed her immune system to fight her melanoma.

In a third trial, Dr. Ernstoff's team gave Carolyn an immunotherapy treatment comprised of protein injections that triggered cross-cellular communications in her immune system to kill the melanoma cells. Her body responded positively to this therapy. Her melanoma disappeared, and 13 years later she is a cancer survivor—one of nearly 14 million living today in the United States thanks to the work of researchers like Dr. Ernstoff and the clinical trials they run with help from the NIH.

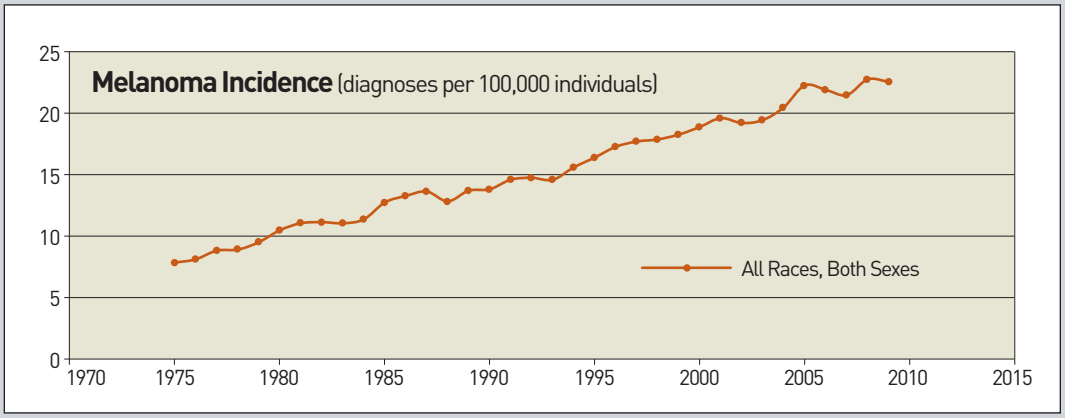
> "Clinical trials saved my life. If I didn't do the clinical trials, I never would have made it."

Carolyn Sumner, stage IV melanoma survivor



Dr. Marc Ernstoff, Dartmouth-Hitchcock Norris Cotton Cancer Center

Even as we make great strides in melanoma treatment, rising incidence rates underscore the urgency for continued research.



Source: U.S. Mortality Data 1975-2008, National Center for Health Statistics, Centers for Disease Control and Prevention

* Has received American Cancer Society funding

Leukemia & Lymphoma

"I feel blessed by having the best medical research team there is, bar none, in the country."

John Hunt, stage IV lymphoma survivor

Rituxan Gets a Stage IV Lymphoma Patient Back to Work

When the prognosis was grim for John Hunt, Rituxan—a drug that targets malignant cells in more than 80 percent of non-Hodgkin lymphoma cases—was the treatment that made a difference.

John was in charge of used car sales for a Chrysler and Jeep dealership in Rochester Hills, Michigan—a job at which he had worked for 23 years—when he was diagnosed with stage IV lymphoma in September 1999. Panic set in. But when an oncologist friend told John that his cancer was curable and advised him to find a good lymphoma specialist, the words gave him the confidence he hoped for.

John's search led to Dr. Mark Kaminski, a federally funded lymphoma researcher at the University of Michigan. Dr. Kaminski recommended a program that included Rituxan. NIH- and NCI-funded clinical trials had yielded many of the key insights that had moved Rituxan from lab to market, including:

- Learning how Rituxan makes a malignant cell sensitive to chemotherapy drugs
- Identifying Rituxan's common side effects of mild fever and nausea
- Proving Rituxan's effectiveness: 46 percent of patients treated with only Rituxan and 95 percent treated with a Rituxan/chemotherapy combination went into remission

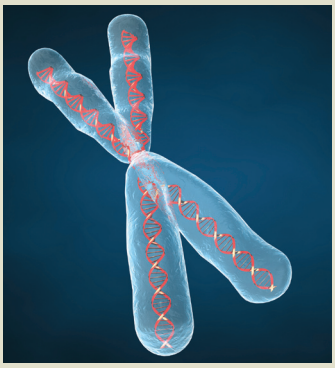
John received eight monthly treatments of Rituxan. Today, his cancer is only a memory, and he is back to doing what he's done for decades—working hard and selling cars.

Bexxar Gives Lymphoma Patients Options

For lymphoma patients who don't respond well to chemotherapy, another drug, Bexxar, offers an alternative by harnessing an element more commonly associated with the energy industry: radioactive iodine.

A breakthrough finding by NCI-funded researchers set the wheels in motion for the development of Bexxar. In 1981, Dr. Lee Nadler and Dr. Stuart Schlossman at the Dana-Farber Cancer Institute developed an antibody (a cancer-identifying protein) that recognized lymphoma cells.

Another team of federally funded lymphoma researchers, led by Dr. Mark Kaminski and Dr. Richard Wahl at the University of Michigan, targeted cancer cells using antibodies tagged with radioactive iodine—with encouraging results. In the initial clinical trials, roughly half of the patients treated experienced complete remission. A subsequent study revealed a five-year survival rate of 65 percent for patients who used Bexxar as their first lymphoma treatment.



Gleevec—A Lifesaving Drug Decades in the Making

Software engineer Manny Ortiz is one of an estimated 26,000-plus Americans living with or in remission from chronic myeloid leukemia (CML), a cancer that invades the blood and bone marrow. He's also one of the fortunate ones treated with Gleevec. Gleevec's development broke important ground in cancer research by proving that it is possible to halt cancer's progression by identifying and targeting a genetic defect.

Manny was just 31 years old the day he went to the doctor with stomach pain and other symptoms he attributed to long hours at work. Tests confirmed a diagnosis of CML.

Thinking about telling his family "really made me pause for a while," Manny says. But then he learned that his cancer was treatable with new drugs.

"Being told you have cancer is never easy. But being told you're lucky really touched me," he says, "I thought, why me? Why am I lucky?"

After receiving Gleevec, Manny experienced no side effects. In fact, he felt completely healthy—well enough even to participate in the Boston Marathon. Today, he is on his way toward remission (a diagnosis made when all cancer cells have disappeared for a sustained period of time).

The basic science that led to Gleevec began long before Manny was born. In 1960 at the University of Pennsylvania, Dr. Peter Nowell and Dr. David Hungerford first noticed an abnormal 22nd chromosome in patients with CML. NCI-funded researchers took this discovery through key milestones leading to FDA approval of the drug in 2001:

- **Targeting the cause:** Dr. John Groffen at the University of Southern California Keck School of Medicine and Dr. David Baltimore*, then at the Whitehead Institute for Biomedical Research at MIT, helped discover what on the mutated 22nd chromosome was instigating unregulated white blood cell growth. It was the presence of the BCR-ABL protein.
- **Designing specialized equipment:** The laboratories of Dr. Thomas Roberts at the Dana-Farber Cancer Institute, Dr. Helen Piwnica-Worms* at the Washington University School of Medicine, and Dr. Brian Druker* at the Oregon Health and Science University Knight Cancer Institute developed the tools necessary to create CML drugs that target the BCR-ABL protein. Dr. Druker studied a large family of signaling proteins and explored its link to human disease. Through this work, he developed tools that detect the activity of these proteins, which were instrumental in the identification of Gleevec as an effective CML treatment.
- **Making connections in the lab:** Studies at the Whitehead Institute for Biomedical Research, Children's Hospital of Los Angeles, and Dana-Farber Cancer Institute linked the BCR-ABL protein to leukemia in mice. At the Dana-Farber Cancer Institute, Dr. Druker studied how mice with leukemia responded to a variety of compounds, including the one that would become Gleevec.
- **Testing the treatment on humans:** A team at the MD Anderson Cancer Center tested Gleevec on a small group of 20 patients. After five months, nine of the patients showed positive evidence that Gleevec had blocked the BCR-ABL protein and killed leukemia cells.

Today, Gleevec is showing promise for treating several other cancers caused by the BCR-ABL protein, including rare tumors of the gastrointestinal tract and acute lymphoblastic leukemia, a fast-growing cancer of the white blood cells.

* Has received American Cancer Society funding

Leukemia & Lymphoma

Evolving Treatment beyond Chemotherapy

> "Some of the discoveries we've made now on this leukemia are having relevance to patients with breast cancer, lung cancer, colon cancer, and prostate cancer."
>
> *Dr. Thomas J. Kipps, Moores Cancer Center*

Doctors have used chemotherapy since the 1950s to fight cancer, saving and extending the lives of millions. Yet these powerful drugs are far from perfect. The common method of treatment, intravenous administration at a health facility, can be painful and inconvenient for the patient. But far worse, chemotherapy can destroy healthy cells along with cancerous cells—weakening patients and causing pain, nausea, and other debilitating and long-lasting side effects.

Chemotherapy has saved millions of lives, but the question remains: can we find a better and less destructive way to battle cancer?

Dr. Thomas J. Kipps* of the Moores Cancer Center at the University of California, San Diego is one of the researchers seeking answers to this question. Supported by a variety of NIH and NCI grants, he is investigating the potential of immunotherapy and targeted treatments for patients with chronic lymphocytic leukemia (CLL). Such drugs target a specific cancer-causing element, like a protein, and harness the power of a patient's own immune system. This differs from chemotherapy drugs, which try to poison or destroy cancer cells and damage healthy cells in the process.

Incremental gains and interconnected discoveries have moved Dr. Kipps' work forward. "By paying attention to what may be happening within any type of clinical experiment or any odd outcome that results from the experiment, breakthroughs can be made," he says.

For his team, such advancements included identifying:

- Genetic factors and biochemical pathways that contribute to CLL's development and growth
- Ways to hinder CLL's survival in the body
- Ways to use gene transfer to generate anti-CLL vaccines
- Findings that revealed the individualized nature of the disease and its treatment—for instance, Dr. Kipps observed that some patients developed antibodies against CLL and some did not

"We're seeing some very encouraging results right now that are being translated into clinical trials," Dr. Kipps says.

Rich Zarr is a patient in one of these clinical trials. The cattle feed manager from Yuma, Arizona, was successfully treated for stage II CLL with chemotherapy in the mid-2000s. When Rich relapsed in 2011, Dr. Kipps enrolled him in a clinical trial of ABT-199, a drug that fights cancer by blocking the activity of the protein that prevents cancer cells from dying.

* Has received American Cancer Society funding

> **"I feel that this approach—taking oral drugs to target certain proteins of various cancers—is where treatment is going in the future."**
>
> *Rich Zarr, chronic lymphocytic leukemia patient*

Unlike Rich's previous chemotherapy treatments, which were administered intravenously, the clinical trial involved taking ABT-199 pills once a day. But that wasn't the only difference Rich noticed between his two treatment regimens. His red blood cell and platelet counts have stayed within the normal range while he has been taking ABT-199.

"Instead of using napalm-like traditional chemotherapy that kills good and bad cells, these intelligent drugs act more specifically against cancer cells," Rich says.

Federal Funding Helps Great Minds Work Together

Many heads are better than one, especially when tackling an intractable cancer such as chronic lymphocytic leukemia (CLL). That's the idea behind integrated research, the model Dr. Kipps used to establish—with NCI support—the CLL Research Consortium.

Now in its 13th year, the CLL Research Consortium program brings many strengths to the cancer fight, including a collaborative group of high-quality laboratories for performing basic research and a larger, more diverse pool of patients for exploring the effectiveness of drugs in development. As Dr. Kipps emphasizes, federal funding gives CLL Research Consortium investigators the resources to develop economies of scale in research and greater latitude to explore hypotheses, moving discoveries forward.

CLL Research Consortium member institutions include:

- Moores Cancer Center (La Jolla, California)
- MD Anderson Cancer Center (Houston, Texas)
- Ohio State University Comprehensive Cancer Center (Columbus, Ohio)
- North Shore-Long Island Jewish Health System (Hyde Park, New York)
- Dana-Farber Cancer Institute (Boston, Massachusetts)
- Mayo Clinic (Rochester, Minnesota)

Several other sites, including The Sanford-Burnham Medical Research Institute in California, as well as Barts and The London Cancer Centre in the United Kingdom, contribute laboratory work to the CLL Research Consortium's efforts.

Lung Cancer

Genetically Targeted Therapies Carry the Fight Forward

"Translational research connects high-quality basic science and curing people."

Dr. Eric Haura, H. Lee Moffitt Cancer Center and Research Institute

Lung cancer is the second most prevalent cancer and the leading cause of cancer-related death of both men and women in the United States. Every year, the cost of treating this disease exceeds $12 billion.

Complicating the fight against lung cancer and other cancers is the fact that a newly discovered drug may work well for some patients yet have no positive impact—or cause serious adverse side effects—in others.

The development of the drug gefitinib, also marketed as Iressa, is one example of selective success. Initially created to treat lung cancer patients who did not respond to traditional chemotherapy, Iressa seemed promising yet showed mixed outcomes. In a Phase III clinical trial (during which drugs are tested on large groups for safety and effectiveness), Iressa appeared to be no more effective than standard treatment options in lung cancer patients who had previously undergone chemotherapy.

Today, Iressa is used in the United States in a highly targeted fashion for non-small cell lung cancer patients with a mutated epidermal growth factor receptor (EGFR). EGFR is a protein found on the cell surface that causes cells to divide. EGFR at abnormally high (or mutated) levels generates excessive division—and causes cancer.

Federally funded researchers played a pivotal role in directing Iressa to patients with an EGFR mutation. For example, NCI funding supported the work of Dr. Harold Varmus'* team at the Memorial Sloan-Kettering Cancer Center, which discovered EGFR to be a common element among lung cancer patients who had never smoked. Dr. Daniel Haber*, another NCI-funded researcher, moved the story forward. His team at Massachusetts General Hospital and Harvard Medical School sequenced the EGFR gene and linked Iressa's efficacy to a particular EGFR mutation.

More key discoveries in genetically targeted cancer therapy are happening today at Florida's H. Lee Moffitt Cancer Center and Research Institute. There medical oncologist Dr. Eric Haura's* federally funded research has put him at the forefront of lung cancer discovery. Dr. Haura and his team of research scientists and technicians are studying how proteins in lung cancer cells cooperate to drive cell growth and survival. Researchers then use these findings to classify different types of lung cancer and develop targeted therapies.

Dr. Haura's team is working under the support of an NCI SPORE (Specialized Program of Research Excellence) grant. SPORE grants commit special funding to specific areas

* Has received American Cancer Society funding

of need that demand new and innovative ideas and processes. The intention of SPORE funding: to drive the translation of scientific discovery into new clinical practices and lifesaving therapies.

A $10 million SPORE grant is supporting Dr. Haura's lung cancer research over the next five years, and the study of cancer signaling proteins is only one aspect of it.

Dr. Haura's team is also investigating:

- How proteins involved in lung cancer growth affect patient sensitivity to chemotherapy
- The effects of global gene expression (conversion of a gene's information onto messenger RNA and then proteins) and gene mutations on lung cancer patient outcomes
- How vaccines directed against the p53 protein can improve outcomes in small cell lung cancer
- How pulmonary inflammation promotes lung cancer development
- Ways to manipulate the tumor environment to improve immune-based therapy

Xalkori Improves Quality of Life for Florida Father

Pioneering science investigations represent only one part of the H. Lee Moffitt Cancer Center and Research Institute's work. The team also helps bring therapies from the laboratory bench to a patient's bedside.

That is good news for patients like Myron Watts. For months, the 45-year-old husband and father of two had noticed increasing breathlessness and fatigue. A chronic cough soon followed. One December day, when trying to mow the grass at his home in Inverness, Florida, he found he had to stop walking after only 20 feet. When Myron sought medical treatment, his life changed forever. The diagnosis: stage IV non-small cell lung cancer.

Myron immediately went to the H. Lee Moffitt Cancer Center and Research Institute, where he was referred to Dr. Haura.

After standard chemotherapy produced little impact on Myron's tumors, Dr. Haura had him undergo a lymph node biopsy to test for the ALK protein. About 1 in 20 patients with non-small cell lung cancer are ALK-positive.

Myron's ALK protein test came back positive, which made him eligible for Dr. Haura's clinical trial using the drug Xalkori, which had just been approved by the FDA. Xalkori fights non-small cell lung cancer by attacking a specific gene, the EML4-ALK fusion gene, which causes the cancerous tumor to grow and helps it survive.

After the Xalkori treatment, Myron's lung cancer tumors disappeared. His breathlessness and fatigue also decreased substantially. Myron continues to take Xalkori daily and sees Dr. Haura for follow-up visits every two months as maintenance treatment to track the cancer.

Myron's health has improved as a result of the sustained and cutting-edge work of scientists working in laboratories across the country toward a common goal: conquering lung cancer.

The dividends are starting to pay—and they've given new life to people like Myron, who says, "I can ride my motorcycle and mow the lawn with a push mower, which I haven't been able to do for two years."

> **"Compared with the standard chemotherapy treatment, I feel really good."**
>
> *Myron Watts, stage IV non-small cell lung cancer patient*

Lung Cancer

Taxol Keeps Cancer Patient Dancing

"I believe Moffitt saved my life."

Mary Edith Thomas, stage IV non-small cell squamous lung cancer survivor

Faces of Lung Cancer, copyrighted by Photo-Documentary Press, Inc. and exclusively licensed by Moffitt Cancer Center

The development of one powerful drug in the fight against lung and other cancers began in 1962, when the NCI contracted with U.S. Department of Agriculture researchers to look for possible cancer-fighting agents in nature. In the early 1970s, Dr. Monroe Wall (NCI-funded from 1970 to 1990) was part of the team that deciphered the molecular structure of a compound derived from Pacific yew tree samples. The resulting drug, Taxol, went on to become perhaps the best-known cancer drug originating from a natural product.

Another NCI-funded researcher, Dr. Susan Horowitz at the Albert Einstein College of Medicine in New York, discovered Taxol's ability to disrupt cell division and multiplication. The NCI also was instrumental in Taxol's Phase I clinical trials. In these trials, researchers at Johns Hopkins University saw 30 percent of patients with advanced ovarian cancer respond positively to the drug.

This work led to FDA approval and vital treatment for patients like Mary Edith Thomas. When Mary Edith learned she had stage IV non-small cell squamous lung cancer in 2005, she was shocked because she had never smoked. But she faced her diagnosis with the same focus and energy she brings to travel and ballroom dancing, two of her favorite hobbies. When told she had less than a year to live, she responded: "I don't think so."

With advice from her doctors, Mary Edith went for aggressive treatment at the H. Lee Moffitt Cancer Center and Research Institute and with an oncologist in her hometown of Melbourne, Florida, who had completed his residency at the center. One of 39 NCI Comprehensive Cancer Centers, the H. Lee Moffitt Cancer Center and Research Institute receives grant support from the NCI, which helps it attract funding from other sources and the best international physicians and scientists.

Mary Edith received a combination of Taxol and traditional chemotherapy, which reduced her cancer by almost half and allowed her to go to work on most days. After two more rounds of treatment and one surgery, Mary Edith has been cancer free for six years and is back to dancing.

If the cancer comes back, she says she'll be first in line to volunteer for a clinical trial. "No hesitation. That is the way researchers learn, and we are the only people who can do it for them. Patients have to be a part of the process."

Tarceva—a Targeted Therapy for an Active Life

A 42-year-old resident of Westbrook, Maine, Sherri Kelley enjoyed walking, biking, skiing, and spending time with her husband and four sons. In 2010, her migraines and debilitating pain led doctors to discover two bleeding tumors in her brain. The diagnosis: stage IV lung cancer that had also spread to her liver, her lymph nodes, and her bones. Doctors didn't expect her to survive.

After surgery to remove the brain tumors, the medical team treated Sherri with Tarceva—a therapy that, like Iressa, targets cancers with high levels of EGFR or mutated EGFR.

Also like Iressa, Tarceva owes its existence to discoveries made by federally funded research. In addition to supporting the pioneering EGFR research by Dr. Harold Varmus and Dr. Daniel Haber, NCI funding also supported the clinical trials that made it possible for Tarceva to be used and administered effectively in Sherri's treatment. These trials not only demonstrated Tarceva's efficacy in specific patient groups, but they also helped researchers home in on maximum dosage levels, effective treatment combinations and the correlation of the appearance of a rash with better outcomes.

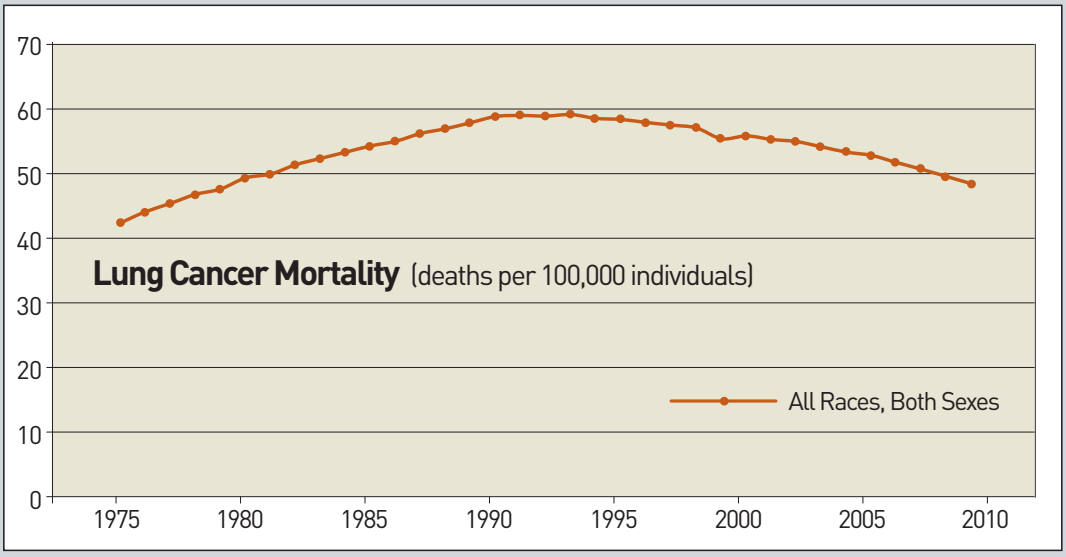
Sherri was on Tarceva for about 14 months. Though she experienced side effects, she says her quality of life remained high. Within five months after surgery, she was able to get back to biking, some running, and even skiing.

"I didn't feel like I really had cancer for all those months because of Tarceva," she says. Sherri is finished with radiation and chemotherapy and is now only on chemotherapy maintenance every three weeks. "I really feel as though I'm kicking this thing," she says.

> **"I really feel as though I'm kicking this thing."**
>
> *Sherri Kelley, stage IV non-small cell lung cancer patient*

Tarceva, a drug developed with the support of NCI-funded clinical trials, keeps Sherri Kelley on the go.

Despite declining lung cancer mortality rates, the need remains high for lifesaving treatments.



Source: U.S. Mortality Data 1975-2008, National Center for Health Statistics, Centers for Disease Control and Prevention

Breast Cancer

Interconnected Findings Lead to Herceptin—and Hope

The NCI Clinical Trials Cooperative Group Program engages more than 3,100 institutions, more than 14,000 individual investigators, and more than 25,000 new patients in specialized clinical trials for cancer treatments each year.

Lisa Bender, pictured here 26 weeks pregnant, is alive today thanks to Herceptin, a drug the NCI Clinical Trials Cooperative Group Program helped to make reality.

Roughly a quarter of all breast cancer patients have a larger-than-average amount of the receptor known as human epidermal growth factor receptor 2 (HER2). Basic research led to the development of Herceptin, a drug that attaches to the HER2 protein and activates immune cells in the cancer fight.

Herceptin helped Lisa Bender achieve the happy family life she enjoys today. In 2010, Lisa was a fit 32-year-old who frequently biked to her job at the Minnesota Department of Health. She was three months pregnant and looking forward to the birth of her first child when she was diagnosed with stage II breast cancer.

Despite her shock, Lisa knew what she wanted. She wanted aggressive treatment. She wanted to deliver a full-term baby. And she wanted a miracle.

Lisa found her miracle in the Masonic Cancer Center at the University of Minnesota. Her oncologist, Dr. Douglas Yee, explained her treatment options, the risks, quality of life issues, and the science behind his recommendations. These recommendations took into account her situation as a pregnant, premenopausal woman who wanted to grow her family.

Herceptin was ruled out while Lisa was pregnant, but she was able to begin a regimen of Herceptin and Taxol three weeks after her daughter was born.

Today, Lisa is undergoing hormone therapy, which is standard in many breast cancer cases. She feels healthy and optimistic enough about the future to eventually try for another baby. She considers Herceptin her "miracle drug" because it doubled her chances of survival. In addition, out of all her treatments, "Herceptin has had the least impact on my quality of life," she says.

A Chain of Discovery

NCI-funded researchers, studies, and clinical trials were pivotal in Herceptin's discovery and advancement.

NCI funding helped both Dr. Dennis Slamon* at the University of California Los Angeles (UCLA) and Dr. William McGuire* at the University of Texas Health Science Center launch their careers. In 1987, these two doctors and Dr. Axel Ullrich at Genentech discovered a commonality among breast cancer patients with high rates of relapse and low rates of survival: high levels of the HER2 protein. At the NCI, Dr. Pier Paulo di Fiore and Dr. Stuart Aaronson demonstrated that

* Has received American Cancer Society funding

HER2 triggers normal cells to take on many of the properties of aggressive tumor cells.

Additional NCI-funded investigators used these findings to explore potential treatments for HER2-positive breast cancer. Dr. Larry Norton at the Memorial Sloan-Kettering Institute for Cancer Research explored combinations of chemotherapy and HER2 antibodies. Dr. Richard Pietras at UCLA strengthened a common chemotherapy drug with HER2 antibodies, which effectively reduced cancer cell growth.

In 2006, after a series of clinical trials administered through the NCI Clinical Trials Cooperative Group Program, the FDA approved Herceptin to treat HER2-positive breast cancer.

Herceptin helped new mother Lisa Bender be there for her daughter.

Tigatuzumab Tackles the Triple-negative Challenge

As researchers and industry have made great strides in the treatment of hormone receptor and HER2 receptor-positive breast cancers, triple-negative breast cancers—breast cancer cells that do not have estrogen receptors, progesterone receptors, or large amounts of HER2—remain a stubborn challenge. Triple-negative cancers represent 20 percent of all breast cancers and do not respond to hormonal blocker drugs that target the HER2 protein.

Tigatuzumab, a protein that targets specific receptors in triple-negative cancer cells, is changing this picture. Tigatuzumab kills approximately 85 percent of triple-negative breast cancer cell lines. When combined with chemotherapy, the effect is more profound. This preclinical discovery led to a clinical trial in patients with metastatic triple-negative breast cancer (breast cancer that has spread to other parts of the body).

Dr. Andres Forero, a researcher at the University of Alabama at Birmingham, led the team that discovered and developed tigatuzumab for treating triple-negative breast cancer.

NCI grants have played an important role in Dr. Forero's development as a successful clinical researcher. Early in his career, a K12 Individual Mentored Career Development Award from the NCI helped establish Dr. Forero as a clinical investigator with a strong laboratory background. The NCI-sponsored K30 Clinical Research Training Program gave Dr. Forero the tools to understand translational research, which applies findings from bench research to medical practice.

Additional NCI grants, most importantly the NCI Specialized Program of Research Excellence (SPORE) grant, supported Dr. Forero's laboratory team as they discovered the tigatuzumab protein and developed the drug through animal studies and human clinical trials. Grants from other sources supported clinical trials of tigatuzumab in triple-negative breast cancer patients.

Today, tigatuzumab is being tested for safety and effectiveness in Phase III clinical trials. More than 130 patients sought to enroll in the most recent trial, according to Dr. Forero.

> "I didn't want to be in private practice—I love translational research: moving science from the bench to the patient."

Dr. Andres Forero, University of Alabama Birmingham

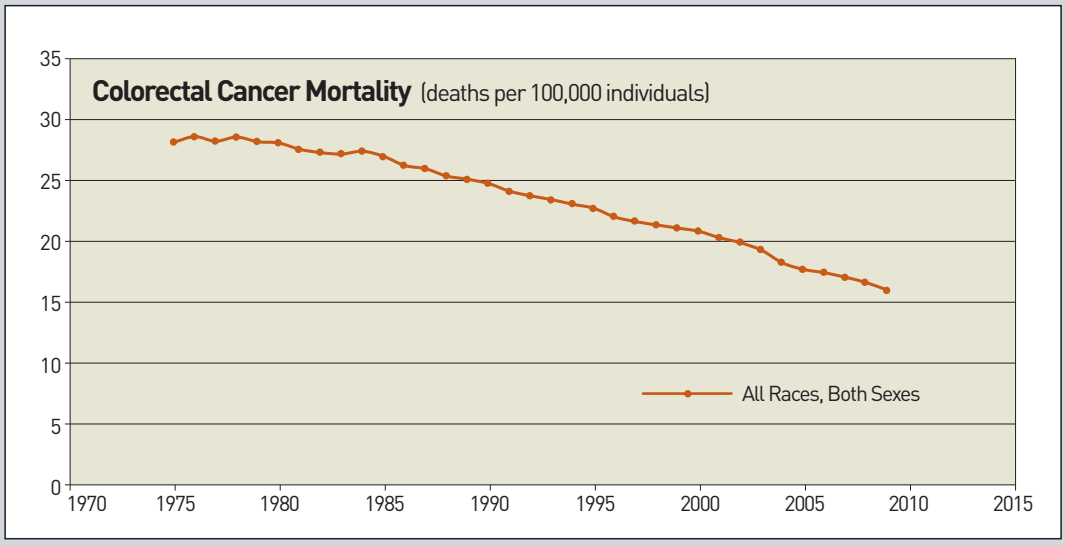
Colorectal Cancer

The overall lifetime risk of developing colorectal cancer (cancer that begins in the colon or rectum) is about 1 in 20. It is the third most commonly diagnosed cancer for men and women in the United States (excluding melanoma) and ranks among the top three causes of cancer-related deaths for both sexes in this country.

The American Cancer Society estimates that, in 2012 alone, more than 143,000 people were expected to be diagnosed with colorectal cancer and that more than 51,000 were expected to die from the disease.

Yet the colorectal cancer mortality rate (number of deaths per 100,000 people per year) has been dropping for more than 20 years due to several factors. Screening is enabling polyps (precancerous growths) to be removed before they develop into cancer. Screening also allows cancer cells to be detected earlier, when the disease is easier to cure. In addition, colorectal cancer treatments have improved over the past several years. As a result, more than 1 million colorectal cancer survivors are alive today.

Since 1975, fewer Americans have been dying of colorectal cancer.



Source: U.S. Mortality Data 1975-2008, National Center for Health Statistics, Centers for Disease Control and Prevention

> “Dr. Folkman’s idea today seems somewhat simple—namely that cancers need blood vessels to grow and that, if we block that process, we can essentially starve the tumor or at least slow its growth rate. Go back a couple decades, and this idea was heretical and revolutionary.”
>
> *Dr. Len Lichtenfeld, Deputy Chief Medical Officer, American Cancer Society*

Avastin’s Powerful Approach to Tackling Tumors

The drug Avastin battles cancer on two fronts: strengthening a patient’s immune system against cancer cells and starving tumors of the oxygen and nutrition they need to grow.

Avastin’s story began in 1971 at Harvard Medical School with research by the late Dr. Judah Folkman*. A pioneer in his field who had been funded by the NCI since 1970, Dr. Folkman observed that tumors signal their need for nutrients by secreting growth factor proteins that stimulate the growth of new blood vessels. This finding laid the groundwork for years of research and discovery.

In 1983 at Harvard, Dr. Harold Dvorak and Dr. Donald Senger—both consistently supported by the NCI since the mid-1970s—connected the high production of a specific protein to malignant tumors. Another group led by Dr. Napoleone Ferrara at Genentech linked this particular protein to angiogenesis, the formation of new blood vessels that tumors need to grow and spread. By the 1990s, clinical trials using anti-angiogenesis treatments confirmed this connection.

Guided by these advances, researchers began developing and testing the angiogenesis-inhibiting drug that would become Avastin—with very encouraging results. For instance, adding the drug to standard chemotherapy treatments increased median patient survival time by 30 percent and increased the median time that a patient’s cancer stopped growing by 71 percent. The FDA subsequently approved Avastin in 2004 as a treatment for colorectal cancer.

Dr. Judah Folkman’s research into tumor behavior laid the groundwork for many of today’s cancer drugs.

* Has received American Cancer Society funding

Colorectal Cancer

Elaine Larsen

Mary Jo Grand

> "If that clinical trial hadn't been available, I would not be here right now."
>
> *Mary Jo Grand, stage IV non-small cell lung cancer patient*

Avastin Shows Promise against Other Cancers

The work that Dr. Judah Folkman began has now resulted in no fewer than six FDA-approved drugs for cancer and applications for FDA approval for treatments targeting many other diseases.

Avastin specifically has been examined in more than 30 NCI-funded clinical trials to fight conditions such as lung cancer, renal cell carcinoma, pancreatic cancer, and ovarian cancer. And the findings have been encouraging so far.

For Elaine Larsen and Mary Jo Grand, Avastin delivered new hope.

Elaine was one of only five or six people in the world with an extremely rare stomach carcinoid tumor, and her treatment had not been going well. More than half of her stomach had been removed. Then the cancer progressed to stage IV, moving into her liver. Chemotherapy, radioactive beads—none of these measures worked.

In early 2009, Elaine felt she had nothing to lose, so she and her oncologist chose to start her on a dose of Avastin every three weeks. "I was an experiment," Elaine says.

And the experiment returned amazing results. Avastin is keeping her tumors in check, and she has returned to volunteering in her community, including at a local church and a nursing home.

Research saved Elaine's life. She says she always knew research was important, but she hadn't realized its true impact on people like her until she got sick and needed help. "I thoroughly, thoroughly believe in research," she says.

So does Mary Jo Grand. When she was diagnosed with stage IV non-small cell lung cancer, she felt like she had received "a punch in the gut." But she was lucky enough to live near the University of Michigan and the Karmanos Cancer Institute. Her oncologist enrolled her in an aggressive six-month clinical trial of Avastin and two other drugs that shrank the tumor on her lung and eliminated all cancer in her lymph nodes.

For two years, Mary Jo continued with biweekly doses of just Avastin. Today, tests reveal no evidence of disease, and she takes Avastin every three weeks with few side effects. "I feel healthy. Avastin and the clinical trial gave me back some of the control that cancer had taken from me," she says. "It put the power back in my hands."

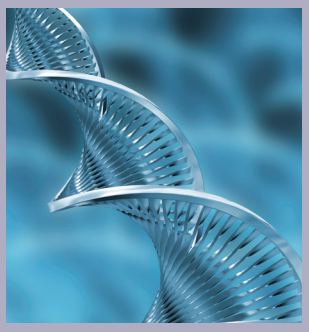
Erbitux—behind a Major Drug, a Cooperative Effort

NCI grants provided steady, long-term support to researchers involved in the development of Erbitux, a powerful treatment in the fight against colorectal cancer, and to the clinical trials needed to bring the drug to patients across the United States.

- Dr. John Mendelsohn* at the MD Anderson Cancer Center, with NCI support, was among the first to propose inhibiting the epidermal growth factor receptor (EGFR) as a way to prevent colorectal cancer cells from getting the nourishment needed to multiply quickly.
- Dr. Paul Harari* at the University of Wisconsin Carbone Cancer Center, also NCI-funded, contributed to the initial research demonstrating Erbitux's power as an EGFR inhibitor, as well as the drug's ability to make cancer cells more sensitive to radiation.
- Dr. Colin Dinney at the MD Anderson Cancer Center, also with NCI support, moved Erbitux research from laboratory mice to human cells.

The National Cooperative Drug Discovery Groups program, one of the first programs to encourage partnerships between the NCI and private industry, engaged several private-sector firms in Erbitux's commercialization. Erbitux received FDA approval in 2004 and is currently widely available to colorectal cancer patients in treatment.

Genetic Testing Helps Match Patients to Treatments



Erbitux, an EGFR-inhibiting drug, works for roughly 60 percent of colorectal cancer patients. How can a doctor know if a patient will benefit from the drug? Test for the KRAS gene. If this gene is normal, the patient will respond to Erbitux. If the gene is mutated, the drug will not be effective. Approved by the FDA in 2009, the KRAS gene test for colorectal cancer was the first genetic test to guide a cancer treatment choice.

* Has received American Cancer Society funding

Cervical Cancer

A Journey from Detection to Prevention and Treatment

Donna Dewson

> "Heather never wanted another girl or woman to go through what she had to go through."
>
> *Donna Dewson, sister of Heather Lyn Martin, who died of cervical cancer in 2005*

More than 12,000 American women are diagnosed with cervical cancer every year. In May 2005, Heather Lyn Martin was one of them. She was diagnosed with stage III cervical cancer at the age of 28. Before the end of that year, she had lost her battle with the disease.

Over a six-month period, Heather's eight-centimeter tumor doubled in size and spread to her lungs and bones. "She had a bad reaction to chemo and radiation and a hard time getting to treatment because she was so sick from it," says Donna Dewson, her younger sister.

Heather chose not to undergo a hysterectomy, another treatment option, because she wanted to have children someday. Sadly, her promising life was cut short before the opportunity arose for her to try any experimental therapy.

"Heather wanted her story to get out there because she never wanted another girl or woman to go through what she had to go through," Donna says.

The leading cause of cervical cancer is infection with a virus known as HPV (human papillomavirus). HPV is a group of more than 100 related viruses that can infect cells on the surface of the skin, genitals, anus, mouth, and throat. Evidence of HPV is found in nearly all cervical cancers.

Over the past several decades, significant advances in cervical cancer screening and prevention dramatically reduced incidence and mortality rates. Breakthrough findings by a series of international researchers provided the groundwork, and subsequent discoveries by federally funded researchers carried the ball forward. The culmination of this work has been the development of the Gardasil vaccine, brought forward by the private sector as one of the first-ever vaccines that can be widely used to prevent cancer from occurring.

In the 1950s, the Papanicolaou test, named after the Greek pathologist who discovered it and now commonly known as the Pap test, revolutionized the outlook for cervical cancer by detecting abnormal or cancerous cells in the uterine cervix, which led to earlier treatment and better outcomes for women.

The German scientist Dr. Harald zur Hausen began researching the role of viruses in cancer in the 1970s and pursued the idea that HPV played a role in cervical cancer. In the early 1980s, Dr. zur Hausen singled out HPV 16 and 18, the strains responsible for about 70 percent of cervical cancers worldwide. In 2008, he was awarded the Nobel Prize for Medicine for his work. Dr. zur Hausen's research opened the door to the development of a vaccine that could prevent the majority of strains of HPV responsible for cervical cancer.

The Pap test has helped reduce cervical cancer mortality in the United States by more than 70 percent since 1955.

Dr. Doug Lowy, NCI Center for Cancer Research

In 1991, Australian researchers discovered that certain HPV proteins could, if shaped in a certain way, provoke a patient's immune system to recognize HPV and produce antibodies to fight it. These particles would not infect a patient because they did not contain virus DNA.

These HPV discoveries laid the foundation for pivotal work by researchers in the United States. In 1992, a Georgetown University research team identified a substance, the L1 protein, which could stimulate the creation of these HPV-fighting particles. The team included Dr. Bennett Jenson and Dr. Richard Schlegel, both of whom received funding from the NCI.

But how could researchers create the L1 protein in the lab? In 1992, Dr. Doug Lowy and Dr. John Schiller at the NCI Laboratory of Cellular Oncology used a virus similar to HPV to create L1 proteins. These triggered large amounts of HPV-fighting antibodies when injected into laboratory animals. Dr. Robert Garcia, also funded by the NCI, successfully repeated this process in humans.

Once HPV had been identified as a key cause of cervical cancer, the NCI researchers developed a vaccine that would trigger an immune response. The next step: clinical trials conducted by the private sector.

Gardasil, the drug that resulted from this research, was approved by the FDA in 2006 for young women and in 2009 for young men. This vaccine has been shown to be highly effective in preventing the majority of cervical cancers.

Yet work remains in the fight against cervical cancer. Current HPV vaccines do not protect women against the high-risk virus types found in some 30 percent of cervical cancers. And, of course, preventive vaccines like Gardasil can't help patients already diagnosed with cervical cancer.

Researchers are exploring a wide range of remedies to this problem, from topical treatments made from seaweed extract to the use of messenger RNA molecules, which provide the blueprint for genes that are made into proteins. Because HPV infections cause so many kinds of cancer, NIH teams are making multi-cancer vaccines a priority as well.

Still other investigators are developing vaccine formulations that are less costly to make and more adaptable for use in the worldwide public health environment. For example, work is proceeding on vaccines that would be usable in countries where refrigeration is unavailable.

Funding Fosters Innovation, Collaboration

"Long-term resources and the freedom to work on high-risk projects" are two reasons why Dr. Doug Lowy has worked at the NCI for 37 years and currently serves as the deputy director of the NCI Center for Cancer Research.

For 14 of those years, he worked with an international team on the development of the HPV vaccine. Dr. Lowy cites two factors that have made his journey possible: federal funding and the ability to collaborate with talented colleagues in France, the United Kingdom, and around the world.

Advances across Diseases

Innovative Tools for Improved Testing

> "Without reliable and standardized assay controls, a patient test result might be reported as 'negative' in one laboratory when in fact the assay itself is not operating as it normally should."
>
> *Dr. Steven Bogen, Tufts Medical Center*

Histopathology—the microscopic examination of tissue—was long considered a task that had to be done by hand. But Dr. Steven Bogen* argued for the advantages of standardizing and automating this complex lab procedure.

Laboratories typically use leftover tumor samples as controls when testing cancer biopsies. However, these tissue samples vary, hindering the accuracy of potentially lifesaving test results. A reproducible measure was needed to ensure consistency among them. With NIH funding, Dr. Bogen and his team at the Tufts Medical Center set out in 1999 to develop a technology that would do just that.

Within three years, Dr. Bogen's team had developed the means to create standardized test samples that could withstand laboratory solvents and be coupled to glass microscope slides. Yet the treatment used to preserve tissue samples was compromising the accuracy of test results. Dr. Bogen identified the chemical changes behind the problem and developed commercial test controls to address them.

Three NIH grants totaling $3.5 million supported Dr. Bogen's initiative from concept development through pilot manufacturing and clinical trial. "The project would not have happened without NIH funding," he says. "It was too risky for private investment capital."

According to Dr. Bogen, "Once commercialized, these standardized test controls will provide a better tool to help ensure patients are diagnosed the same, regardless of where their biopsy is evaluated. If we're successful, the technology will 10 years from now become a standard of care for this type of testing."

Perfect Timing for a Multipurpose Treatment

When her cancer returned, George Blough (pictured here on the left with her husband, Brooke) got a second chance with Taxol.

When cancer made an unwelcome reappearance—in an unexpected place—for George Blough, a drug that treats multiple types of cancers made the difference.

George was first diagnosed with ovarian cancer in 1990 at age 45. A hysterectomy left her cancer free—or so she thought.

Seven years later, breathing troubles indicated that the cancer had returned as metastatic ovarian cancer in her right lung.

George's six rounds of treatment included Taxol, a drug that inhibits cell division in breast, lung, and ovarian cancer and Kaposi sarcoma. Taxol sent her cancer into remission.

Taxol's journey from discovery to powerfully versatile drug culminated just in time for George. Had Taxol not been approved between her first and second battles with cancer, she says, she might not be here today. "It's a good thing my cancer returned after seven years and not any sooner."

* Has received American Cancer Society funding

Public-private Partnerships Create a Versatile Vaccine

Today, a vaccine called Stimuvax is giving colorectal cancer patients—as well as individuals with prostate and lung cancer—new hope by activating their own immune systems against the disease.

Although a pharmaceutical company is developing the drug and conducting the clinical trials, its roots trace back to hundreds of NIH-funded research projects that identified and studied a molecule found in these tumors: MUC1.

"The body of knowledge developed by NIH-funded research on MUC1 served as the integral building blocks for this vaccine," says Dr. Helen Sabzevari of EMD Serono, Inc., recognizing the publically supported bench science that often precedes private-sector development of new drugs and therapies.

"Early on, the research was so high risk that no one in the field was doing it other than scientists at NIH," she says.

As global head of oncology and immunotherapy at EMD Serono, Dr. Sabzevari leads the company's efforts to develop therapeutic vaccines like Stimuvax. "Collaboration between the NIH and private industry is critical to the advancement of research and patient care," she says.

> "If funding for the NIH is not sustained, we would be taking away chances from our patients."
>
> *Dr. Helen Sabzevari, EMD Serono, Inc.*

Grants Support Careers—and Patient Care

Can an intensive treatment, like a bone marrow transplant, be made easier for young cancer patients? Shouldn't palliative care—which focuses on relief from symptoms, pain, and stress—be used at every stage of treatment for pediatric patients, not just at the end of life?

The answer to these questions is yes. Supported by an NIH career development grant, Dr. Christina Ullrich is finding ways to improve the way cancer care is delivered to young patients. At the Dana-Farber Cancer Institute, she's studying young people undergoing bone marrow transplants who are showing high levels of disrupted sleep and fatigue.

Her goal: to build a body of evidence-based research and best practices to help such patients, and it's an area with tremendous potential impact. Two-thirds of children diagnosed with cancer today will endure life-threatening side effects, as well as long-lasting damage from their cancer treatment. Palliative care helps alleviate this suffering for these patients and their families.

In this research project, federal funding is not only enhancing our nation's ability to deliver better quality care to cancer patients and survivors, but it is also opening up new ways to deliver better care at a lower cost—the essence of health care delivery reform.

NIH funding is helping Dr. Christina Ullrich find ways to improve the treatment experience for cancer patients of all ages.

An Investment with Returns for Life

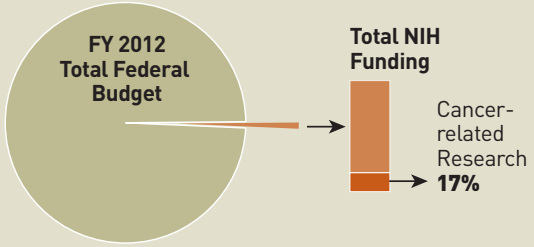
The stories in the preceding pages only scratch the surface of the contributions federally funded basic research has made and continues to make in the fight against cancer.

As a nation, we have made remarkable progress since President Nixon declared war on cancer in 1971. Today, scientists are taking that 41-year foundation of work and exploring the genetic origins of the disease. They're giving doctors new options of personalized treatment for individual patients. And they are on the cusp of a whole new era of discovery in the fight against cancer.

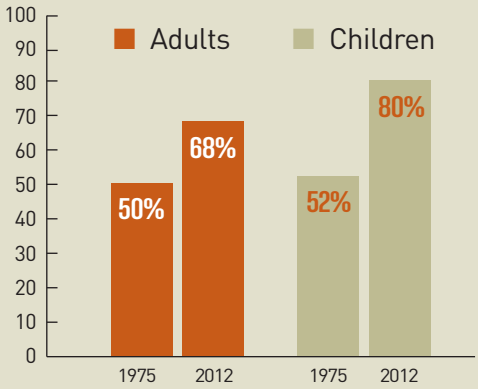
The mapping of the human genome by NIH-funded researchers more than a decade ago opened up new frontiers in molecular biology, immunology, protein studies, and personalized medicine. And we're only starting to realize the benefits of these advances.

Between 1990 and 2007, the rate of death from cancer decreased by 22 percent for men and 14 percent for women. Over that time, nearly 900,000 fewer people died from the disease. These individuals are our beloved family members, friends, neighbors, co-workers, teachers, and so many others whose lives are so meaningful and whose contributions are so important. Nearly 14 million cancer survivors in the United States are alive today thanks to the advancements in science and medicine made possible by federally funded basic research.

NIH funding represents less than 1 percent of the entire federal budget. Only $5.4 billion a year of this funding fuels cancer research.



More people diagnosed with cancer today are expected to live five years or more after diagnosis.



Source: The American Cancer Society

And there are other, less obvious benefits as well. Federally funded research powers the American economy. In 2011, $23.6 billion in NIH-supported medical research generated $69 billion in other new economic activity, creating and supporting nearly 433,000 high-paying jobs in every state.

An Ecosystem We Can't Afford to Abandon

Federally funded basic research is an investment with compounding returns. According to the National Bureau of Economic Research, each dollar committed to research by the federal government generates 32 cents in private medical research investment.

As shown in this report, research projects supported by the NIH and NCI, and the discoveries they yield, are essential to the work of centers like the Mayo Clinic, the Dana-Farber Cancer Institute, the MD Anderson Cancer Center, and academic research institutions across the country. Government-funded basic research and clinical trials are essential to the process of drug research, development, and testing conducted by the private pharmaceutical industry. It is a public-private partnership that successfully brings new therapies to more patients and saves more lives every year.

America's commitment to research has created whole new economies of scale in the cost of fighting cancer. No private entity could have undertaken the cost of unraveling the human genome. But the NIH did—with a project that helped to lower the cost of sequencing the human genome from $100,000 to just under $8,000.

Momentum We Can't Afford to Lose

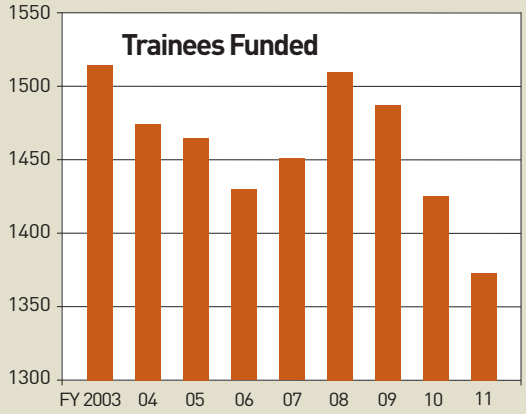
Despite its clear importance and overwhelming value, federally supported basic research is not immune from the fiscal challenges facing the nation. Over the past decade, the NCI's budget has remained static. Meanwhile, inflation and the rising prices of technology and equipment have reduced the NIH's purchasing power by more than 17 percent, and the cost for the NCI is even greater.

Fewer than 13 percent of applicants for NCI research grants today successfully receive support, compared with 28 percent just 10 years ago. The average age of a first-time NCI grant recipient increased five years (from 37 to 42 years old) between 1980 and 2007.

Because of this diminishing support, some researchers will leave the field entirely—and the lifesaving potential of their research may never be realized. Others will find a way to work in countries such as China, Korea, and Singapore—nations that are committed to leading the world in biomedical research and drug development.

For more than half a century, the United States has led the world in biomedical research, and the world's best scientists have worked here. As this report has demonstrated, the resulting advancements in the fight against cancer—and the benefits of a robust economic sector based on medical research, development, and technology—have been quantifiable and indisputably positive.

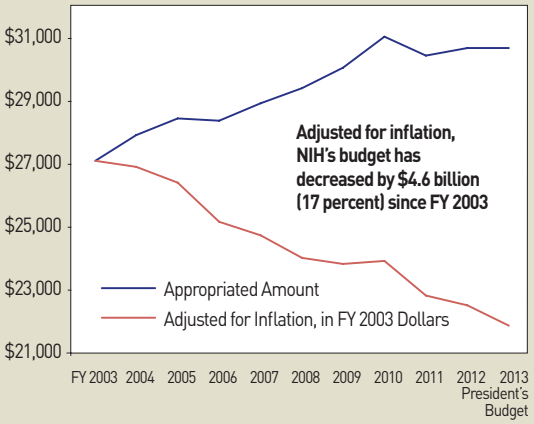
Support is slipping for the next generation of researchers.



Source: The National Cancer Institute

Shrinking budgets slow the cancer fight.

NIH Appropriations FY 2003-2013
(in millions)



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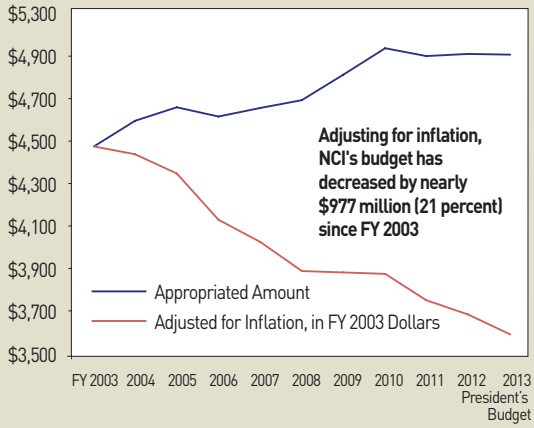


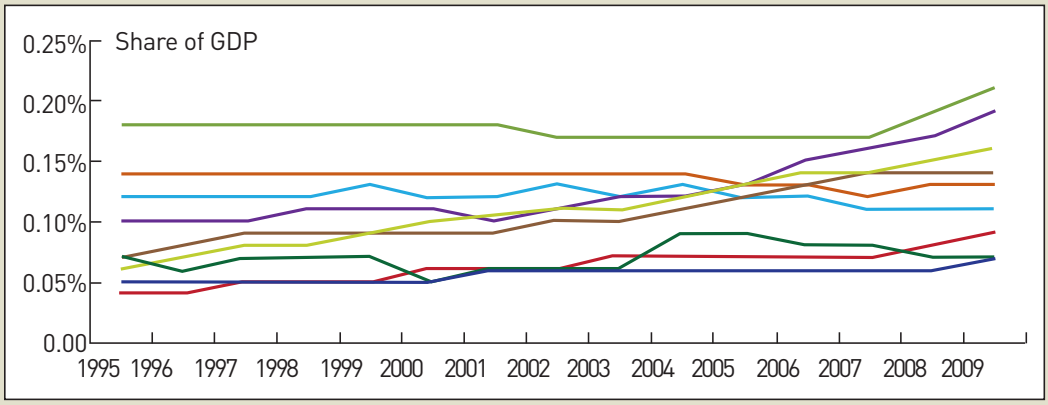
Leadership We Can't Afford to Cede

Will we lose our global leadership in cancer research and innovation?

Today, the NIH Clinical Center is the world's largest clinical research hospital, and the NCI is the largest source of early stage cancer funding in the United States, supporting experienced and new investigators alike.

America's pioneering initiatives in cancer research have made us a leader. We cannot put that position at risk.

U.S. government-funded medical research and development lags behind many other industrialized nations.



Source: The Information Technology and Innovation Foundation and United for Medical Research

Progress We Can't Afford to Halt

Cancer costs the United States more than $226 billion annually in terms of medical expenses and lost productivity due to illness or early death. Despite recent advancements, cancer incidence rates are currently projected to nearly double by 2020. Because cancer is primarily a disease of the aged, the incidence of cancer increases as the population grows older and lives longer. By 2030, Americans over the age of 62 are expected to represent 70 percent of cancer diagnoses.

Is our nation prepared? When considering this question, we must remember one statistic that trumps them all: about one-third of all women and one-half of all men are expected to develop cancer in their lifetimes.

More powerful, innovative, and effective methods of early detection and treatment are within reach. But we must maintain our dedication to discovery—and that work depends on a robust commitment to research that only the federal government can make and sustain over time.

Federally Funded Research Strengthens America—from Coast to Coast

Jobs Supported by NIH Awards to States, FY 2011

State	NIH awards ($M)	TOTAL EMPLOYMENT
Alabama	268.5	5,373
Alaska	9.2	453
Arizona	183.8	4,532
Arkansas	62.6	1,786
California	3,535.3	63,196
Colorado	320.3	6,372
Connecticut	479.5	6,504
Delaware	30.6	508
District of Columbia	202.4	544
Florida	492.6	12,993
Georgia	463.3	10,963
Hawaii	60.7	1,390
Idaho	9.3	449
Illinois	779.2	14,960
Indiana	216.2	5,028
Iowa	197.7	4,217
Kansas	105.8	2,128
Kentucky	156.3	3,680
Louisiana	166.8	4,397
Maine	74.9	1,821
Maryland	1,687.7	24,557
Massachusetts	2,507.9	34,598
Michigan	655.5	11,744
Minnesota	493.8	9,209
Mississippi	33.9	1,191
Missouri	477.3	7,489
Montana	39.7	960
Nebraska	84.1	1,787
Nevada	20.6	901
New Hampshire	88.4	1,396
New Jersey	250.7	5,352
New Mexico	105.7	2,037
New York	2,041.4	33,193
North Carolina	1,063	20,571
North Dakota	17.5	453
Ohio	711	14,886
Oklahoma	82.5	2,650
Oregon	303.6	6,089
Pennsylvania	1,455.1	24,291
Rhode Island	152.8	2,395
South Carolina	142	3,560
South Dakota	18.6	397
Tennessee	479.9	9,360
Texas	1,066.8	25,878
Utah	171	4,132
Vermont	52.6	1,067
Virginia	332.3	6,376
Washington	926	15,180
West Virginia	19	721
Wisconsin	402.6	8,036
Wyoming	6.2	349
50 states plus D.C.	23,704	**432,099**

Source: United for Medical Research

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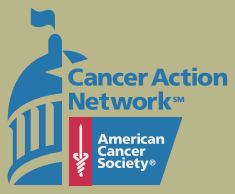
Most importantly, we would like to extend our heartfelt gratitude to all the people who took the time to share their stories with us.



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