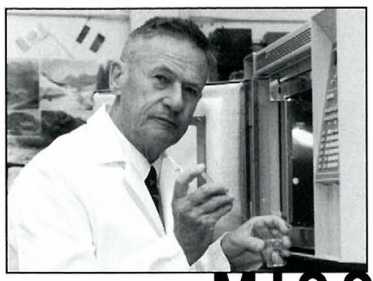
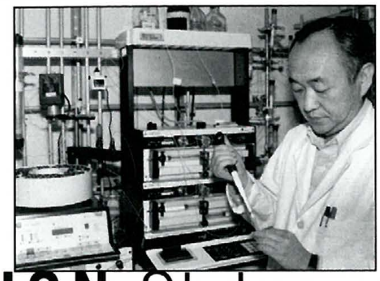
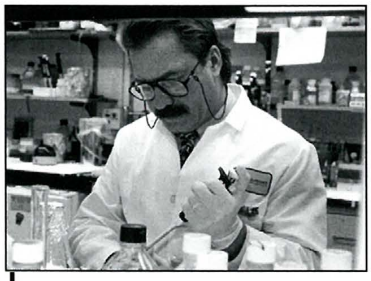
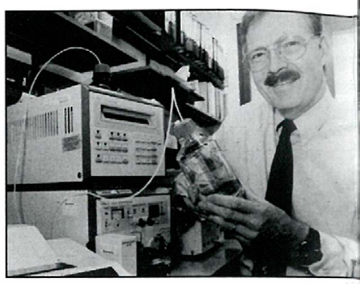

National Foundation for Cancer Research
research for a cure
laboratory without wall

MISSION Statement

The National Foundation for **Cancer Research** (NFCR) was founded in 1973 to support cancer research in the laboratory. NFCR research conducted at both the cellular and molecular levels is leading to better prevention, earlier diagnosis, new treatments, and eventually a cure for cancer. By supporting the best ideas of the best minds and by facilitating collaboration among NFCR Project Directors, advances in one field contribute to discoveries in another. This is what NFCR's **"Laboratory Without Walls"** makes possible.

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Photos above (left to right): Keith Ingold, Ph.D.; Yung-Chi Cheng, Ph.D.; Wayne Marasco, Ph.D.; and Helmut Sies, M.D.

1999 President's Message

As you look through the pages of our latest Annual Report, I think you will agree 1999 was a time of great innovation and achievement for the National Foundation for **Cancer Research** (NFCR).

NFCR President Franklin Salisbury, Jr. (right) confers with Project Director Don Engelman.

From gaining a greater understanding of the genetic events that unleash skin cancer, to improving the effectiveness of breast cancer treatments, to learning how we can literally choke tumors of the critical blood supply they need to grow, the past year was filled with many important cancer research advances thanks to NFCR scientists.

Like you, I believe our progress speaks volumes about our Project Directors and their commitment to innovation and developing pioneering approaches that will revolutionize cancer prevention and treatment, and ultimately stop this disease from taking lives.

Yet I cannot highlight the successes of our scientists without offering my thanks and appreciation to NFCR's valued donors. Indeed, it is the generosity of our supporters—and their willingness to sponsor discovery research and imagine a world where no one has to live in fear of cancer—that powers and sustains our efforts to eliminate our nation's second leading killer.

In this regard, the achievements of the National Foundation for **Cancer Research** will always be shared by our scientists, supporters, and the cancer patients who benefit from the lifesaving advances made by our Project Directors.

However, until NFCR realizes our singular goal of eradicating cancer in our lifetime, we cannot turn away from the research challenges standing between us and a cure.

That is why those of us who have joined together to stop cancer must rededicate ourselves to supporting the best minds and the most promising research so that we can alleviate the pain of millions of cancer patients and their loved ones.

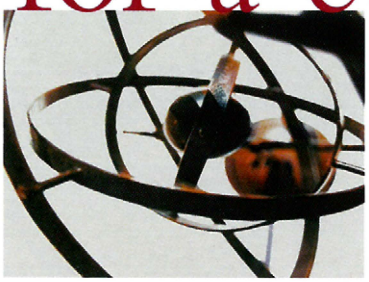
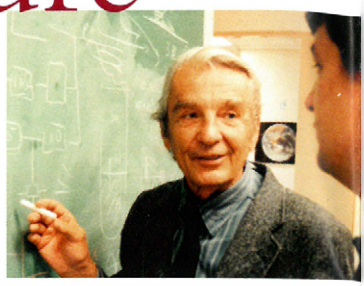
Working together, we will succeed.

Sincerely,

Franklin C. Salisbury
President

research for a cure



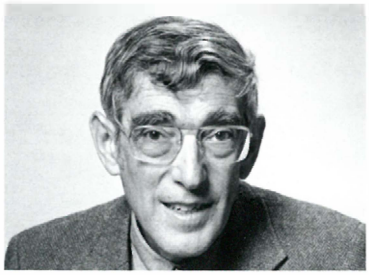



Merging the Basic Sciences in a Spirit of Innovation and Achievement

The National Foundation for Cancer Research sponsors laboratory research that seeks to save lives by understanding what causes cancer at its most fundamental level.

Our dedication to this kind of discovery-oriented research—which merges the basic sciences of mathematics, physics, and chemistry—is driven by our commitment to realizing the day when cancer no longer threatens the lives of men, women, young and old alike.

On the pages that follow, we invite you to share in the innovations and achievements of our Project Directors, and to join us in honoring those whose lives have been touched by cancer.



PROJECT DIRECTOR

Bruce Ames, Ph.D.
NFCR Project Director since 1984

AFFILIATION

Professor of Biochemistry and
Molecular Biology
University of California-Berkeley

NFCR RESEARCH FOCUS

"Vitamins B12 and Folic Acid in Cancer Prevention"

Investigating the role of vitamin B12 in minimizing DNA damage in humans as an extension of our previous work on folate deficiency as a major contributor to DNA damage.

SELECTED PROFESSIONAL ACHIEVEMENTS

U.S. National Medal of Science, 1999

Joseph Priestley Award, 1998

Medal of the City of Paris, 1998

Developed the *Salmonella* liver test for mutagenicity, 1974

Basic Science Studies Connect Nutrition to Cancer Prevention & Detection

While studies have shown that as many as one-third of cancer cases result from a poor diet or low consumption of fruits and vegetables, what is not fully understood is which foods and in what quantities are most effective at reducing a person's risk for developing cancer.

That is why NFCR Project Director DR. BRUCE AMES of the University of California-Berkeley conducts important research to achieve a more complete understanding of the role that diet and nutrition play in the onset and prevention of cancer.

Specifically, Dr. Ames focuses on the impact micronutrients have on an individual's cancer risk. Micronutrients are vitamins, minerals, and other elements found in the foods we eat that are critical to keeping the human body and its vital systems functioning and healthy. With support from NFCR, Dr. Ames is identifying the optimum levels of key micronutrients that people need to consume in order to improve their diets and reduce their likelihood for developing cancer.

"By targeting funding in special areas, and through its efficient administration, NFCR has made a significant impact on cancer research and is an excellent illustration of why private charity has an important role to play in cancer science funding." —BRUCE AMES, PHD

In his research, Dr. Ames has pinpointed nine micronutrients that, when consumed in the proper amounts, appear to play a key role in preventing cancer—folic acid, vitamin B12, vitamin B6, niacin, vitamin C, vitamin E, iron, zinc and selenium.

Furthermore, Dr. Ames has tied folic acid deficiency to the development of colon cancer. In short, he has uncovered the mechanism that leads to cancer-causing DNA damage when a person consumes too little folic acid, a vitamin found in fruits and vegetables. By developing a method to detect this genetic damage, Dr. Ames has made it easier to predict which individuals are most likely to develop the chromosomal breaks on DNA that can result in colon cancer.

In the future, Dr. Ames' research will be directed at fine-tuning the Recommended Daily Dietary Allowances published by the government, particularly as they relate to cancer-fighting nutrients like folic acid, and vitamins B12 and B6. With continued support from NFCR, he also hopes to expand his research to study the role other nutrients play in cancer prevention and development.

Above: Daniel Von Hoff, M.D.

Photos, page 2: I. Bernard Weinstein, M.D. (far left); Ivar Giaever, Ph.D., Nobel Laureate (far right)

research for a cure

"The wonderful thing about NFCR support is its continuity and flexibility. I can count on it to…start an interesting new project that another granting agency may consider 'risky.' It is an important safety net for my laboratory, for which I am very grateful." —KATHRYN HORWITZ, PHD

PROJECT DIRECTOR

Kathryn Horwitz, Ph.D.
NFCR Project Director since 1984

AFFILIATION

Professor of Endocrinology and Molecular Biology
University of Colorado Health Sciences Center

NFCR RESEARCH FOCUS

"The Molecular Biology of Progesterone Action in Breast Cancer"

Studying how female hormones influence the growth of some cancers will result in new laboratory tests for earlier detection and higher cure rates for breast cancer.

SELECTED PROFESSIONAL ACHIEVEMENTS

President, Endocrine Society, 1998/99

President's Special Commission on Breast Cancer, 1992/93

National Institutes of Health MERIT Award, 1992

Researcher Improves Effectiveness of Breast Cancer Treatments

The drug tamoxifen has garnered much attention as one of the most effective treatments against breast cancer. To achieve its results, tamoxifen blocks receptors in the breast for the female hormone estrogen, which is known to stimulate rapid cell division and tumor growth.

Unfortunately, evidence exists that in some women breast cancer tumors may actually become resistant to tamoxifen and resume their growth after initially shrinking in size.

Faced with this dilemma, NFCR Project Director DR. KATHRYN HORWITZ at the University of Colorado Health Sciences Center researches the role female hormones such as estrogen and progesterone play in transforming tumor-fighting drugs like tamoxifen into substances which actually promote the growth of malignant cells.

The presence of estrogen receptors has long been an important predictor of whether tamoxifen will be an effective treatment for a breast tumor. Yet through her research, Dr. Horwitz determined that another female hormone —progesterone—is an even better indicator of whether a tumor will respond favorably to tamoxifen.

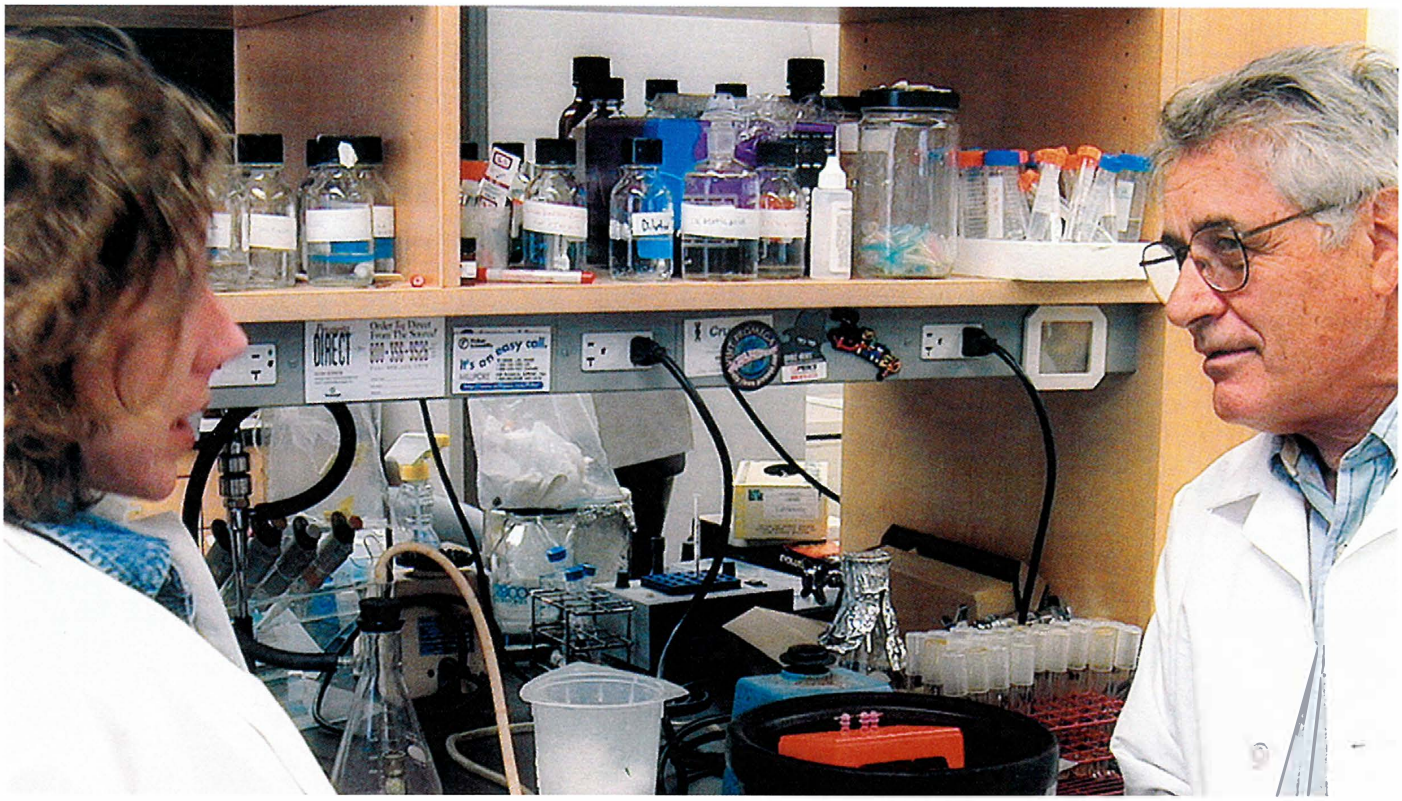
As a result of her findings, pathologists can now conduct tests to determine if both estrogen and progesterone hormone receptors are present in a tumor.

The presence of both receptors indicates that estrogen receptors are working properly and will therefore respond to tamoxifen treatment without becoming resistant to the medication over the long term. In fact, 80 to 90 percent of breast tumors with both progesterone and estrogen receptors react favorably to tamoxifen.

With these results in hand, Dr. Horwitz is now turning her attention to developing new ways to increase the level of tumor-fighting proteins in hormone receptors. These special proteins can repress tumor growth, and could increase the effectiveness of tamoxifen since the drug could be administered for longer periods without patients building up a resistance to the medication.

Backed by NFCR, Dr. Horwitz has made significant contributions to the understanding of breast cancer and traditional therapies. In addition to developing a reliable way to predict which tumors will respond to tamoxifen, her work may soon lead to improved treatments and higher cure rates by identifying other tumor fighting agents.

Below (right): Hector DeLuca, Ph.D.



research for a cure

"The philosophy of NFCR has been to find research which is delving into the root problem [of cancer] as opposed to peripheral issues. This is the most important issue related to funding by NFCR [and] it can explain why so many of the investigators supported by NFCR are recognized as the world's leaders in cancer research." —DANNY WELCH, PHD

PROJECT DIRECTOR

Danny Welch, Ph.D.
NFCR Project Director since 1995

AFFILIATION

Associate Professor of Pathology
Pennsylvania State University College of Medicine

NFCR RESEARCH FOCUS

"Regulation of Metastasis in Human Cancer"

Identifying the presence of genes that suppress the ability of breast cancer cells to metastasize and evaluating how these genes are regulated by hormones and how these genes work.

SELECTED PROFESSIONAL ACHIEVEMENTS

National Research Award,
National Institutes of Health, 1988

Member, American Association for the Advancement of Science

Member, American Association for Cancer Research

New Progress in Containing the Deadly Spread of Skin Cancer

Most cancers can be beaten if they are detected in their earliest stages and treated promptly. In fact, estimates indicate that nearly ninety percent of cancer patients would survive their illness if they could be treated before their tumors metastasize, or travel to other parts of the body.

To help stop cancer's deadly spread, NFCR Project Director DR. DANNY WELCH and his team at the Pennsylvania State University College of Medicine are investigating the genetic mutation in malignant cells that they believe enables a tumor to metastasize at such rapid speed.

In planning his work, Dr. Welch knew from research conducted by other scientists that tumor tissue taken from metastatic or secondary locations in the body frequently lacked pieces of chromosomes, which direct the activities of human cells. In particular he focused on research that described this phenomena in melanoma, which is a common form of skin cancer.

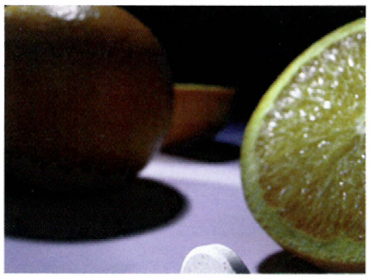
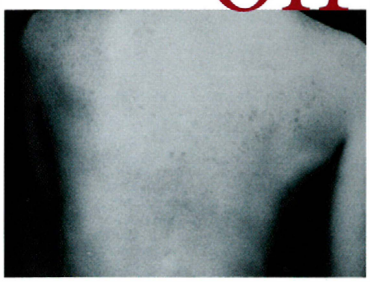
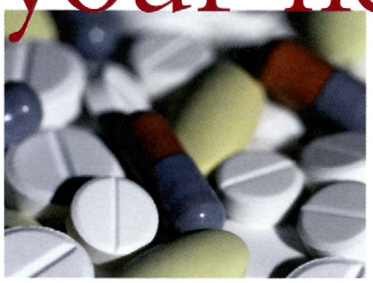
Building on this knowledge, Dr. Welch found that by replacing the missing chromosomes, he could eliminate melanoma's ability to metastasize. Even more promising, he determined that within the damaged chromosomes, a gene called KiSS-1 helps block metastasis in melanoma.

Left: Danny Welch, Ph.D.

In short, Dr. Welch's research showed that the KiSS-1 gene was deactivated in the melanoma cells that had the ability to spread, suggesting that KiSS-1 might function to suppress metastasis. Further investigation revealed that when KiSS-1 was "turned on" in melanoma cells, it prevented metastasis at least fifty percent of the time.

Looking to the future, Dr. Welch will attempt to understand precisely how the KiSS-1 gene works in suppressing metastasis. With the ongoing support of NFCR, his research efforts will focus on determining ways to reactivate the metastasis-fighting KiSS-1 gene, and to prevent it from deactivating when it is exposed to melanoma cells. By understanding how KiSS-1 functions, Dr. Welch will be able to formulate drugs that help stop the spread of melanoma.

on your health


There is an enormous amount of information available about ways to reduce your risk for cancer. But with so many sources providing confusing and often contradictory guidance on how to live a longer, healthier life, it is difficult to separate the good advice from the bad.

So to help you live a happier, healthier life, the National Foundation for **Cancer Research** believes it is important to keep you up-to-date with helpful and informative tips that you and the people you care about can use to reduce your risk of getting cancer.

That is why NFCR has prepared this list of **50 Easy Ways to Reduce Your Cancer Risk.** Try one of these tips each week for the next year and you will significantly cut your cancer risk—and improve your overall health and fitness.

50 Easy Ways to Reduce Your Cancer Risk

Nutrition

WEEK 1: Eating five to nine servings of fruits and vegetables a day makes up a healthy diet plan. Apples, oranges, corn and carrots are healthy and popular choices for many Americans.

WEEK 2: Too much fat in a person's diet is suspected to increase the risk of heart disease, as well breast, prostate, and colon cancer. To reduce your fat intake while enjoying the foods you love, choose leaner cuts like fish, chicken and turkey instead of only red meat.

WEEK 3: Eating fiber-rich foods like fruits, vegetables, and whole grains may be a way to reduce your risk for colon cancer. Soups like lentil and minestrone also offer a wholesome way of providing your body with the hearty fiber it needs to stay healthy.

WEEK 4: Crucifers, or vegetables like cabbage, broccoli, brussels sprouts, and turnips are nutritional powerhouses. Not only do they add flavor to your meals, they stimulate the immune system, and help protect against colon, stomach, and respiratory cancer.

WEEK 5: If you are worried about pesticides on fruits and vegetables, simply wash your produce thoroughly before eating. Or consider buying organically grown fruits and vegetables.

WEEK 6: Cooking techniques such as broiling, grilling, roasting and baking provide a low-fat alternative to frying or sautéing. To add variety to your menu, try cooking your favorite foods using one of these healthier alternatives.

WEEK 7: Try low-fat alternatives: use skim or 1% milk instead of whole milk, spread mustard instead of mayonnaise on your sandwich, and buy tuna packed in water rather than oil.

WEEK 8: Breakfast truly is the most important meal of the day. Begin your morning with a fiber-rich cereal with your favorite fruit and skim or 1% milk.

WEEK 9: Don't overcook vegetables. Cooking veggies too long and at too high a temperature can remove cancer-fighting vitamins, minerals, and nutrients from produce.

WEEK 10: You can't possibly avoid every carcinogen. Fortunately, vegetables offer us natural defenses. Onions and garlic contain allyl sulfides, which may help the body process cancer-causing chemicals more safely.

WEEK 11: When you're in a hurry, use your microwave to cook cancer-fighting vegetables. Studies show that vegetables cooked in the microwave retain 80-100% of their nutrients.

WEEK 12: Make chicken even healthier by removing the skin before or after cooking.

WEEK 13: Use olive oil as a bread spread. It is a good source of unsaturated fats and provides a healthier alternative to the saturated fats of butter and margarine.

WEEK 14: Curb between-meal cravings with healthy, delicious, cancer-fighting snacks by keeping fresh fruit, cut vegetables, applesauce and other dried fruits in your kitchen.

WEEK 15: Enjoy the health benefits of baked potatoes. Instead of topping them with high-fat butter, margarine, or sour cream, try non- or low-fat yogurt or salsa on your spuds.

WEEK 16: Tomatoes, especially in ketchup and tomato sauce, contain a powerful anti-cancer pigment called lycopene that may lower your risk for developing cancer.

WEEK 17: When buying pasta or bread, make sure it includes whole wheat, bran, rye or oatmeal to maximize the amount of fiber in the foods you eat.

WEEK 18: Keep packets of raisins handy for munching on a healthy high-fiber snack.

WEEK 19: Consuming Vitamin C in foods such as orange juice or in supplement form may help prevent mouth, esophageal, lung, stomach, and colon cancers.

WEEK 20: Eating foods high in the provitamin beta carotene (like carrots, yams, and mangoes) may suppress the cancer process in cells that have been exposed to carcinogens.

WEEK 21: Too busy to add fiber? Try these quick fiber fixes: add chickpeas or kidney beans to your next salad, or add vegetables like tomatoes or cucumbers to your lunchtime sandwich.

WEEK 22: Be sure to drink plenty of fluids—at least eight cups a day—to help prevent bladder cancer.

WEEK 23: When it comes to preventing breast cancer, what you drink is just as important as what you eat. So women at high risk for breast cancer should consider avoiding alcohol.

WEEK 24: Potassium is important for proper cell functioning. A breakfast of grapefruit juice and fresh strawberries topped with yogurt gives you nearly one-third of your daily potassium.

WEEK 25: Popular fruits like grapes have special cancer-fighting properties. In fact, red grapes may inhibit blood vessel growth, the body's last line of defense against a tumor.

Fitness & Exercise

WEEK 26: Maintain a healthy body weight with exercise. Being overweight can contribute to cancers of the breast, colon, and endometrium (the lining of the uterus).

WEEK 27: Walking is a great way to boost your energy level and decrease your cancer risk. If you're just starting out, try walking five minutes a day, then work up to ten minutes after a week or so, building your time in five-minute increments thereafter.

WEEK 28: If you choose walking as your exercise, make sure you have a good pair of walking shoes. They cushion your feet, absorb shock, and reduce the strain on your joints.

WEEK 29: To maintain your flexibility and to help prevent stiffness following a workout, stretch and warm-up for at least five minutes before and after your exercise.

WEEK 30: Avoid injury—consult your physician before beginning any exercise program.

WEEK 31: Listen to your body. If you feel pain while exercising, stop. To relieve minor aches, try increasing your warm up time. For chronic pain, consult your physician.

WEEK 32: To lose weight, exercise 40 minutes a day, five days a week. To maintain a healthy body weight, exercise 30 minutes per day, five days a week.

WEEK 33: Having trouble finding time to exercise? Try a 45-minute walk, cycle, or swim at lunch.

WEEK 34: Don't limit yourself to aerobic exercises like walking or swimming. Strength training, like lifting weights or exercising against resistance, can make bones stronger, improve balance, increase muscle strength and mass, and improve overall health.

WEEK 35: Here's a helpful hint to keep in mind when working out: If you can't talk and exercise at the same time, you are going too fast.

WEEK 36: Exercise doesn't have to include a trip to the gym. Regular activities like gardening can provide significant health benefits, especially for senior citizens.

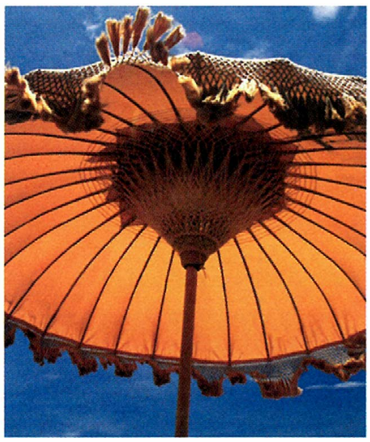
WEEK 37: Exercise with a friend. It is a great way to stay motivated when you don't feel like working out.

WEEK 38: If you have difficulty exercising for the recommended 30 minutes per day in a single stretch, try breaking your exercise routine into shorter, more frequent blocks of time that are more manageable, like three 10-minute periods per day.

Health & Wellness

WEEK 39: More than 80% of lung cancer cases are related to smoking tobacco. If you don't smoke, don't start. And if you do, quit. It's the best way to reduce your risk for many cancers.

WEEK 40: Schedule regular cancer screenings. Women age 40 and over should have an annual mammogram to check for breast cancer, while men age 50 and over should be examined for prostate cancer with a PSA blood test.



WEEK 41: Overexposure to the sun's ultraviolet rays has been linked to the 1 million skin cancer cases diagnosed in the U.S. each year. Protect yourself by using a sunscreen with an SPF (or sun protection factor) of 15 or greater.

WEEK 42: Many of the most popular sunscreens are not waterproof. Reapply sunscreen if you are involved in water activities, or if you have been exercising enough to perspire.

WEEK 43: When out in the sun, wear a wide brimmed hat to protect the back of your neck, your ears, and your face from harmful exposure to the sun.

WEEK 44: Early detection is a woman's best defense against breast cancer, so protect yourself. Women age 20 and over should conduct monthly self-breast examinations.

WEEK 45: Visit your doctor for an annual physical and overall health evaluation. Be sure to speak up about any symptoms. Your doctor can't help you if you don't tell him or her.

WEEK 46: Watch for these seven warning signs of cancer. If you have any of these symptoms, it does not necessarily mean you have cancer. Consult your doctor for a thorough check-up.

- Change in bowel or bladder habits
- A sore that does not heal
- Indigestion or difficulty in swallowing
- Thickening or lumps in breast or elsewhere
- Obvious change in wart or mole
- Unusual bleeding or discharge
- Nagging cough or hoarseness

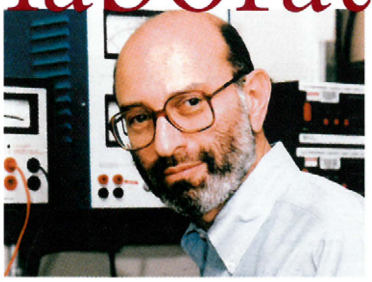
WEEK 47: Women should see their gynecologist for annual pap smears to screen for cervical cancer.

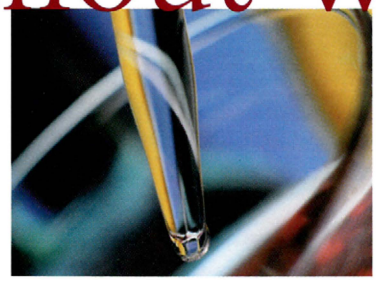
WEEK 48: To fight skin cancer, check your skin at least once a month for new moles that have changed in color, shape, or size. Consult your physician if you find a suspicious blemish.

WEEK 49: Men should conduct frequent self-exams for testicular cancer, examining their testes for irregular lumps or growths.

WEEK 50: Know your family's cancer history. Research has shown that colon, prostate, breast, and skin cancers can be inherited. Talk to your doctor about possible tests to determine your risk if you have family members who have been afflicted by cancer.

laboratory without walls






Linking the Best Cancer Scientists in Our Laboratory Without Walls

Chances are that you or someone you know has been affected by cancer, which will soon surpass heart disease to become the leading killer in America. That is why NFCR fosters cooperation among scientists and enables them to share discoveries in a "Laboratory Without Walls" that unites the best minds and the most forward-looking research so that we can cure cancer in our lifetime.

With more than 1,500 Americans losing their battle with cancer each day, our "Laboratory Without Walls" speeds research progress and gives our scientists the power to take a promising idea from the lab to the bedside where it can benefit a cancer patient and save a life.

PROJECT DIRECTOR

Kenneth Kinzler, Ph.D.
NFCR Project Director Since 1999

AFFILIATION

Professor of Oncology
Johns Hopkins Oncology Center

NFCR RESEARCH FOCUS

"Novel Approaches to Identifying Cancer Chemotherapeutics"

Studying the sequence of genetic events that lead to cancer and developing methods to analyze how genes function to form protein such as Serial Analysis of Gene Express (SAGE).

SELECTED PROFESSIONAL ACHIEVEMENTS

Institute for Scientific Information
Superstar of Biomedicine, 1998

John Hopkins University
Sandoz Award, 1988

Alumni Award, Philadelphia College of Pharmacy and Science, 1983

Research Breakthrough Raises Prospect of Stopping Colon Cancer Before it Starts

Each year, an estimated 56,000 Americans lose their lives to colon cancer. And while scientists have long suspected that many individuals are born with a hereditary predisposition to contract colon cancer, little progress has been made in discovering the primary genetic mutation responsible for passing this deadly disease from one generation to the next.

That is why NFCR Project Director DR. KENNETH KINZLER of the Johns Hopkins University Oncology Center has launched a groundbreaking research initiative to shed new light on the complicated events surrounding the genetic change responsible for the onset of colon cancer.

In his search for colon cancer's genetic "gatekeeper," Dr. Kinzler has

identified a gene called APC. When APC is in its normal form, it suppresses tumors. However, when it mutates, APC loses its cancer-fighting ability and allows malignancies to develop.

Furthermore, Dr. Kinzler ascertained in one study that APC mutations existed in over 80% percent of the colon cancer patients he examined. Likewise, similar results were found in patients with Familial Adenomatous Polyposis, a condition that leads to colon cancer.

"For much of the 'war on cancer,' the molecular causes of cancer have been completely unknown. The recent revolution in molecular genetics has allowed the definition of specific genetic alterations that drive the development of cancer. Knowledge of these changes now, for the first time, allow the truly rational development of anti-cancer drugs." —KENNETH KINZLER, PHD

Even more telling, Dr. Kinzler determined that when APC mutates, it no longer regulates the death of cells in the colon and instead allows growths that can become cancerous to form. So clearly, APC plays a central and perhaps the primary role in initiating colon cancer.

By identifying the exact mutations that are critical to the origins of colon cancer, Dr. Kinzler has opened the door to finding new ways to interrupt the onset of this and many other types of cancer. In particular, his identification of the genetic gatekeeper for colon cancer—the APC gene—creates a cellular target that could be used to "turn off" cancer before it starts.

On another front, Dr. Kinzler's work could lead to the development of treatment and prevention agents that target specific defective genes. These new medicines may be more effective and less toxic than existing chemotherapy compounds currently in use.

Photos, page 12: Stanley Cohen, M.D. (far left); Alanna Schepartz, Ph.D. (far right)

laboratory without walls

"We can't explain the majority of these [leukemia] cases as there is no family link. However, we have shown that by studying genetics we may get clues to the environmental cause, in this case, the lack of folate, which allows us to intervene and prevent the disease." —MARTYN SMITH, PHD

PROJECT DIRECTOR

Martyn Smith, Ph.D.
NFCR Project Director Since 1990

AFFILIATION

Professor of Toxicology
University of California-Berkeley

NFCR RESEARCH FOCUS

"Genes Involved in Leukemia"

Discovering genes associated with susceptibility to acute leukemia in adults and using folic acid to protect against adult leukemia.

SELECTED PROFESSIONAL ACHIEVEMENTS

National Advisory Environmental Health Sciences Council of the National Institutes of Health, 2000

Fellow, American Association for the Advancement of Science

Member, Society of Toxicology

Folic Acid Discovery Offers Hope for Leukemia Prevention

Scientists have implicated lifestyle choices such as smoking and a poor diet—and causative events such as overexposure to toxic substances—in 80 to 90 percent of all cancer cases.

However, what is less clear is why some people do not develop cancer even if they engage in certain behaviors (like eating a diet high in fatty foods) that should increase their chances of becoming ill. This raises questions about the possibility that some people possess genetic traits that inherently make them more resistant—or susceptible—to cancer.

To gain more insight into this issue, NFCR Project Director DR. MARTYN SMITH is conducting breakthrough research to connect genetic events to the onset of cancer. In particular, he has been at the forefront of efforts to establish the link between folic acid—a vitamin commonly found in green vegetables, fresh fruit, liver, and yeast—and incidences of acute lymphocytic leukemia, which is cancer of the bone marrow.

Earlier discoveries by other scientists showed that folic acid deficiency causes breaks in human chromosomes and increased health risks. Working from this knowledge, Dr. Smith examined a gene called MTHFR that metabolizes folic acid and controls how it is processed in the body. In his research, Dr. Smith determined that individuals with two mutated copies of the MTHFR

gene were up to five times less likely to develop leukemia than people without the mutation.

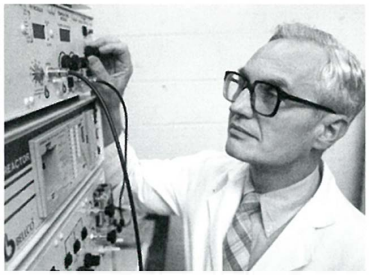
In short, the mutated MTHFR gene changes the way that folic acid is used in the body. Instead of being utilized in other cellular processes, the mutation directs more folic acid towards DNA synthesis. This reduces the chance that dividing cells will suffer the genetic damage that causes them to become cancerous. However, it is estimated that 85 percent of the U.S. population does not carry the MTHFR mutation that can help prevent acute lymphocytic leukemia.

Above: Martyn Smith, Ph.D.

Nevertheless, Dr. Smith and his research team have determined that by consuming more folic acid-rich foods such as leafy, dark green vegetables, beans and peas, oranges, and berries in their diets, individuals could significantly reduce their risk for leukemia and other types of cancer.

laboratory without walls

"One of the advantages of the approach we have taken, that of inhibiting tumor growth, is that it should apply to all types of cancer and therefore might be one type of therapy that would have universal applicability."—HAROLD DVORAK, MD



PROJECT DIRECTOR

Harold Dvorak, M.D.
NFCR Project Director Since 1980

AFFILIATION

Chief, Department of Pathology
Beth Israel Deaconess Medical Center/Harvard Medical School

NFCR RESEARCH FOCUS

"Molecular Recognition"

Identifying the process by which tumors acquire new blood vessels and finding steps by which cancer growth and spread can be halted.

SELECTED PROFESSIONAL ACHIEVEMENTS

President, American Society for Investigative Pathology, 1996-1999

President, New England Society of Pathologists 1997/98

Associate Editor, *Cancer Research*, 1989/90

Researcher Aims to Starve Cancer Tumors

For many years, cancer treatments have focused on medicating the symptoms of cancer, either through surgery to remove the tumor and surrounding tissue, or via radiation and chemotherapy protocols that kill malignant cells, but also damage healthy tissue.

Despite significant improvements in traditional cancer therapies, none of these treatments has been completely effective at curing common breast, prostate, and colon cancers.

That is why DR. HAROLD DVORAK, the Chief of Pathology at Boston's Beth Israel Deaconess Medical Center, is using support and sponsorship from the National Foundation for **Cancer Research** to better understand tumor biology and the process by which cancer cells metastasize, or spread, from their primary location to other parts of the body.

Like all living tissues, cancer tumors need a steady supply of blood to survive. So as a part of his research into tumor biology, Dr. Dvorak focuses on angiogenesis, the process that malignancies use to generate the new blood vessels they need to grow and spread. Dr. Dvorak believes that if he can stop the mechanism by which tumors acquire additional blood vessels, he could prevent tumor growth or metastasis and literally starve tumors to death.

In research supported by NFCR, Dr. Dvorak has pinpointed a molecule called VEGF that causes cancer tumors to emit a clotting agent which

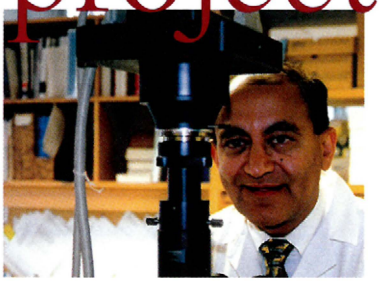
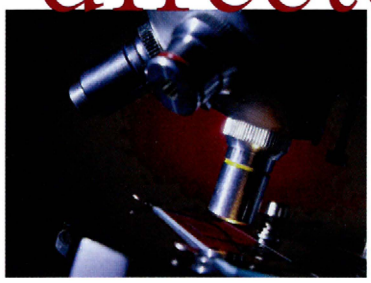
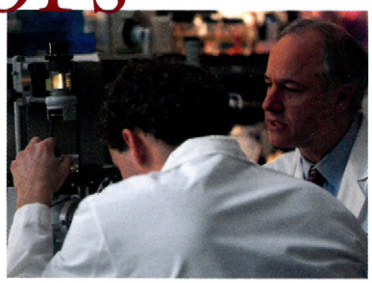
Above: Harold Dvorak, M.D.

encourages and supports the growth of the new blood vessels. However, Dr. Dvorak has also determined that unlike healthy tissue, tumors continually produce VEGF, allowing malignant cells to grow and spread at rapid speed.

Armed with this knowledge, Dr. Dvorak and his research team are now directing their efforts at finding new ways to stop cancer tumors from over-producing VEGF. Once this information is in hand, medical science will be better equipped to offer cancer patients therapies that surpass traditional treatments because physicians will be able to prevent cancer cells from growing and spreading throughout the body.

In addition to this important application, Dr. Dvorak's research could also be used to remedy other angiogenesis-driven illnesses such as rheumatoid arthritis, heart disease, and stroke.

project directors


Bruce Ames, Ph.D., *see page 2*

Jacqueline Barton, Ph.D.
California Institute of Technology
Pasadena, California
"Recognition of DNA Sites with Metal Complexes"
Designing peptides to recognize and interact with specific segments of DNA to regulate gene expression.

Stephen J. Benkovic, Ph.D.
Pennsylvania State University
University Park, Pennsylvania
"Enzymes in Nucleotide Biosynthesis and DNA Replication"
Studying the role of specific enzymes in the production of DNA and RNA.

Esther H. Chang, Ph.D.
Georgetown University
District of Columbia
"Modulation of the Radiation Resistant Phenotypes of Tumor Cells by Sequence Specific Oligonucleotides"
Investigating the molecular basis of tumors being resistant to radiation therapy and developing new therapies to kill cancer tumors that are metastasizing or spreading to secondary locations in the body.

Yung-Chi Cheng, Ph.D.
Yale University
New Haven, Connecticut
"Pleiotropic Drug Resistance-DNA Exonuclease and Telomerase"
Discovering a new DNA (genetic) repair enzyme which may result in new treatments to prevent resistance of cancer cells to anticancer drugs.

Curt I. Civin, M.D.
Johns Hopkins University
Baltimore, Maryland
"Transduction of Human Hematopoietic Stem Cells"
Using the human-immunodeficient mouse (hu/mu) hematopoietic chimera model system to investigate the possibility of using novel conditionally replicating lentivirus vectors for efficient transduction of genes into human hematopoietic stem cells.

Stanley Cohen, M.D.
Stanford University School Of Medicine
Stanford, California
"Genes that Suppress the Growth and Metastasis of Cancer Cells"
Isolating human metastasis genes (MSGs) using the random homozygous knockout (RHKO) approach, specifically focusing on human breast and melanoma neoplasia due to their rapid increase in incidence.

Hector F. DeLuca, Ph.D.
University of Wisconsin-Madison
Madison, Wisconsin
"Vitamin D Analogs as Anti-Leukemia Agents/Biochemical Basis of Chemical Carcinogenesis"
Creating non-toxic forms of Vitamin D for treatment of leukemia and other cancers.

Peter B. Dervan, Ph.D.
California Institute of Technology
Pasadena, California
"Studies in DNA Recognition"
Investigating the chemical basis for the specificity of protein binding to DNA.

Harold Dvorak, M.D., *see page 16*

Donald M. Engelman, Ph.D.
Yale University
New Haven, Connecticut
"Receptor Interactions within Membrane Bilayers"
Studying cancer cell membrane functions which will lead to new and more effective anticancer therapies.

Ivar Giaever, Ph.D., Nobel Laureate
Rensselaer Polytechnic Institute
Troy, New York
"Cell Substrate Interactions"
Studying the interaction of normal and cancer cells and why cancer cells spread and move about the body. Developed an "electrified petri dish" which lets researchers monitor the slightest motions.

Waun Ki Hong, M.D.
M.D. Anderson Cancer Center
Houston, Texas
"Molecular and Genetic Studies of Lung Cancer in Women: Potential Implications for Prevention"
Investigating the biological processes of lung cancer and identifying chemoprevention agents that are effective in preventing lung cancer.

Csaba Horvath, Ph.D.
Yale University
New Haven, Connecticut
"High-Resolution Separation of Glycoconjugates"
Developing novel high performance liquid chromatography columns to investigate various approaches to high performance separation of complex carbohydrates and other biological molecules for early detection of cancers.

Kathryn Horwitz, Ph.D., *see page 4*

Keith U. Ingold, Ph.D.
Steacie Institute for Molecular Sciences
Ottawa, Canada
"Antioxidants in Normal and in Tumor Tissues"
Researching on how the antioxidant vitamins C, E, and betacarotene are used by the body will advance knowledge of how some cancers may be prevented.

Rakesh Jain, Ph.D.
Massachusetts General Hospital
Boston, Massachusetts
"Tumor Pathophysiology"
Developing novel techniques for non-invasive functional lymphatic monitoring and deep tissue imaging.

Kenneth Kinzler, Ph.D., *see page 12*

Sir Aaron Klug, Ph.D., Nobel Laureate
MRC Laboratory of Molecular Biology
Cambridge, England
"Zinc Finger"
Investigating intervention in gene expression by the use of zinc finger proteins which are small DNA binding peptide motifs and the best natural design for targeting DNA.

Janos Ladik, Ph.D.
Universitat Erlangen-Nurnberg
Erlangen, Germany
"Quantum Theory of Proteins and DNA and Their Interactions; Chemical Carcinogens and Radiations Activating Oncogenes and Inactivating Antioncogenes"
Developing an unified theory for the initiation of cancer and investigating the electronic structure of gene systems.

Wayne A. Marasco, M.D., Ph.D.
Dana-Farber Cancer Institute
Boston, Massachusetts
"Mechanism of Transformation of Human Lymphocytes by the HTLV-1 Virus"
Studying the mechanism by which the human T-cell leukemia virus (a retrovirus) transforms

human lymphocytes. This work may lead to the first gene therapy to treat adult T-cell leukemia.

Thomas C. Merigan, M.D.
Stanford University School of Medicine
Stanford, California
"Drug Resistance in Infection with HIV: A Cancer Promoting Virus "
Studying the influence of the protease mutation leading to pan protease resistance and designing strategies for drug therapy.

Cesar Milstein, Ph.D., Nobel Laureate
MRC Laboratory of Molecular Biology
Cambridge, England
"Site-Directed Modification of Genes of the Immune System"
Using gene targeting techniques to develop transgenic mice with genetic mutations suspected of causing human T-cell leukemia.

Ronald Pethig, D.Sc.
University of Wales
Bangor, Gwynedd, Wales
"Electrokinetic Properties and Manipulation of Cells"
Developing a new optical technique which makes it possible to measure and compare the electrical charge differences between cancer and normal cells and bring about more effective strategies for new cancer therapies.

Ilya Prigogine, D.E.S., Nobel Laureate
Instituts Internationaux de Physique
et de Chimie Solvay
Brussels, Belgium
"Modelisation of Cellular Proliferation and Supercellular Morphological Instabilities"
Modeling of anti-cancer cytocidal reactions mediated by T lymphocytes and the morphological stability of cellular tissues.

Terence H. Rabbitts, Ph.D.
MRC Laboratory of Molecular Biology
Cambridge, United Kingdom
"Role of Chromosomal Translocations in Development of Human Cancer"
Developing model systems to investigate many new mutations and discovering possible drug targets.

Manfred F. Rajewsky, M.D.
University of Essen
Essen, Germany
"Chemically-Induced Tumorigenic Conversion in the Developing Rat Nervous System: DNA Modifications and Repair, and Cell Lineage-Specific Gene Alterations"
Detecting specific gene mutations in brain tumors which offers new hope for the development of more effective therapies for these difficult to treat cancers.

Alexander Rich, M.D.
Massachusetts Institute of Technology
Cambridge, Massachusetts
"Nucleic Acid Structure and Carcinogenesis"
Using X-ray diffraction analysis to determine the three-dimensional structure of biological molecules with some considerable emphasis on the nucleic acids, the major information carriers of biological systems.

W. Graham Richards, D.Sc.
Oxford University
Oxford, England
"Design of Anticancer Drugs"
Developing computer graphics which permit the molecular modeling and design of powerful new anticancer drugs to destroy tumor cells without harming other normal tissue cells.

Robert D. Rosenberg, M.D., Ph.D.
Beth Israel Deaconess Medical Center
Boston, Massachusetts
"Role of Heparin Markers in the Regulation of Cell Growth"
Discovering specialized tissue cells which produce heparin-like substances to inhibit or slow tumor cell growth for new strategies of treating cancers.

Leo Sachs, Ph.D.
Weizmann Institute of Science
Rehovot, Israel
"The Reversibility of Malignant Cell Transformation"
Discovering that natural proteins called colony stimulating and maturation factors regulate the growth of white blood cells and can cause blood cancer cells to become normal suggests new approaches to cancer treatment.

Ramaswamy Sarma, Ph.D.
State University of New York at Albany
Albany, New York
"Structure and Dynamics in DNA-Drug Complexes"
Using innovative magnetic resonance imaging technology to study the shape of DNA (genetic) molecules will enhance the development of new and more effective anticancer drugs.

Alanna Schepartz, Ph.D.
Yale University
New Haven, Connecticut
"Non-Natural Metalloregulated, AP-1 Site-Specific DNA Binding Peptides"
Developing a new class of anti-sense molecules to control gene expression and inhibit genes that cause cancer.

Harold A. Scheraga, Ph.D.
Cornell University
Ithaca, New York
"Molecular Recognition"
Investigating the structure and function of growth factors using molecular modeling and NMR analysis. Has solved the 3-D structure of epidermal growth factor.

Paul Schimmel, Ph.D.
Scripps Research Institute
La Jolla, California
"Peptide Motifs for RNA Interactions"
Investigating peptide elements which interact with RNA motifs used in decoding of genetic information.

Pravinkumar Sehgal, M.D., Ph.D.
New York Medical College
Valhalla, New York
"Interleukin-6 in Cancer"
Investigating abnormalities of cytokine signalling in cancer cells and developing active anti-cancer immunotherapy in human cancer.

Helmut Sies, M.D.
Heinrich-Heine-Universitat
Dusseldorf, Germany
"Biological Significance of Peroxidation Reactions"
Obtaining information on how certain antioxidant nutrients (Vitamin E, betacarotene) may prevent certain cancers.

Jeffrey L. Sklar, M.D., Ph.D.
Brigham and Women's Hospital
Boston, Massachusetts
"Molecular Genetic Analysis of Tumor Spread in Malignant Gliomas of the Brain"
Determining pattern of spread in brain tumors by tracing genetic mutations from the primary tumor.

Martyn Smith, Ph.D., *see page 14*

Michael Sporn, M.D.
Dartmouth Medical School
Hanover, New Hampshire
"Triterpenoids and Cancer Prevention"
Identifying chemoprevention targets early in the carcinogenic process and developing new drugs to stop tumor development.

Daniel D. Von Hoff, M.D.
University of Texas Health Science Center
San Antonio, Texas
"Intermediates in Gene Amplification"
Discovering extra chromosomal genetic material (episomes) that can make tumors drug resistant and how hydroxyurea can destroy the episomes.

I. Bernard Weinstein, M.D.
Columbia University
New York, New York
"Carcinogens, Oncogenes, and Human Cancer Causation"
Studying the cellular and molecular mechanisms by which chemicals in the environment and our diet cause cancer.

Danny Welch, Ph.D., *see page 6*

Photos, page 18 (from left to right): Rakesh Jain, Ph.D.; Curt Civin, M.D.; Manfred Rajewsky, M.D.




Public Support and Resource Stewardship

Linking Past and Present to Imagine a World Without Cancer

NFCR was founded in 1973 when Franklin and Tamara Salisbury learned Nobel Laureate Albert Szent-Gyorgyi was unable to find funding for his latest cancer research project.

The world-renowned scientist was rejected by potential funding sources because unlike his contemporaries—who tended to tread on familiar scientific ground—Szent-Gyorgyi could not predict the results of his research. So, inspired by Szent-Gyorgyi's dilemma, the Salisburys sent the scientist a modest check of $25, and asked him to join them in establishing NFCR.

While much has changed since NFCR's founding, one thing has remained constant: the benevolence of the many private individuals who generously support our efforts. So to our donors and supporters who through their generosity imagine a world where no man, woman, or child must face the terrible threat of cancer, we say thank you.

1999 Financials

NFCR is deeply appreciative of all of the financial support that it receives from private donors, foundations, and corporations. However, due to space limitations, we are not able to recognize every gift in this report. Nevertheless, in view of the critical link between our donors, the research initiatives of our Project Directors, and NFCR's mission to cure cancer, we feel it is important to provide our supporters with detailed information regarding our management of their contributions.

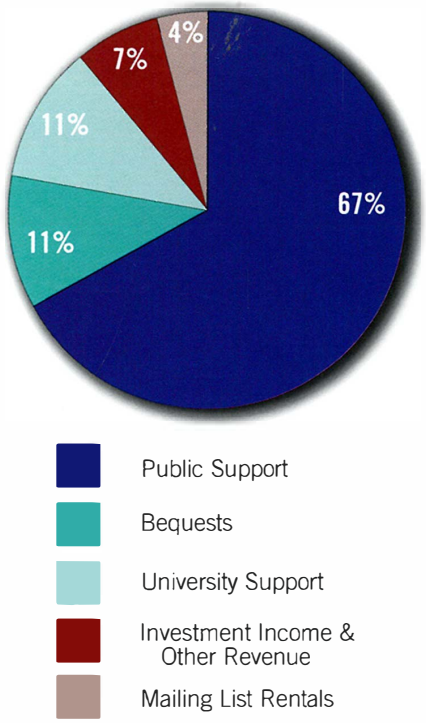
Financial Information for the National Foundation for Cancer Research

Year ending September 30, 1999

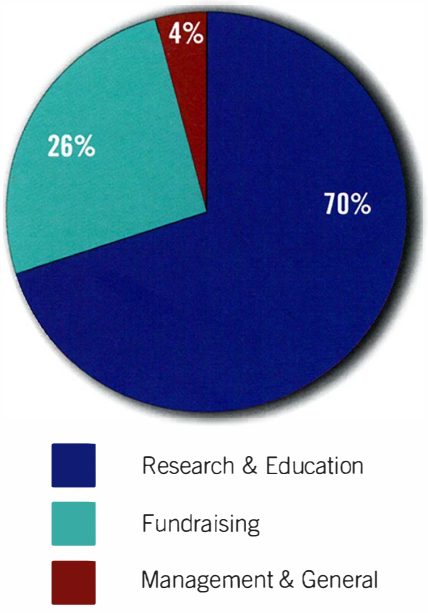
Support and revenue:	
Public support	$ 9,975,658
Bequests	1,732,992
University support	1,740,857
Mailing list rentals	522,846
Net investment income	964,129
Other revenue	27,786
Total support and revenue	14,964,268
Net assets released from restrictions	1,996
Total revenue	14,966,264
Expenses:	
Program services:	
Research	5,966,236
Public education and information	4,296,722
Total program services	10,262,958
Supporting services:	
Fundraising	3,776,076
Management and general	638,296
Total supporting services	4,414,372
Total expenses	14,677,330

To receive a copy of NFCR's Financial Statements and Schedule for September 30, 1999 and 1998 (with Independent Auditor's Report) from the auditing firm of KPMG, please call us at 1-800-321-CURE or go to our website, www.NFCR.org.

FY 1999 REVENUE



FY 1999 EXPENSES



SAMPLE WILL LANGUAGE

A will is the cornerstone of your plan for the future. With a provision in your will for NFCR, you can make a significant investment in a healthy future for your loved ones.

Here is sample language you might use to remember NFCR in your will:

"I give, devise and bequeath to the National Foundation for Cancer Research, a charitable organization incorporated in the state of Maryland with its principal office at 4600 East West Highway, Bethesda, MD $_____ (or _____% of the residue of my estate) to be used for NFCR's basic science cancer research program."

Although the process is simple, you should seek the advice of your attorney to see that your will or codicil is drafted effectively.

Memorial/Honor Gifts

All of us know someone special whom we have admired, respected and loved. We invite you to celebrate that special person's life with a donation made in his or her honor to the National Foundation for **Cancer Research.** Or perhaps you would like to send a memorial contribution instead of sending flowers at the death of a loved one. This is really a gift so others might live—for it goes to support lifesaving cancer research. A handsome card is sent to the honoree, or in the case of a memorial gift, an "In Memory of" card with the name of the donor is sent to the family. We receive so many individual gifts of this kind that space limitations do not permit listing all the honorees. But we are grateful for them all.

If you would like more information about how to contribute through NFCR's Honor/Memorial program, please call us at **1-800-321-CURE** and ask for Ann Mariani.

Planned Giving

Planned giving is an increasingly popular way for donors to make charitable gifts, meet their current income needs, and take advantage of tax incentives. Although NFCR will not realize the benefits of your generosity until the future, your planned gift will have a significant impact on cancer research. By providing us with the financial stability we need to plan for the long term, together we can ensure our Project Directors will always have the support they need. For more information, contact NFCR at **1-800-321-CURE.**

Legacy for A Cure

Many individuals have demonstrated their support to our mission by notifying us of their plan to contribute to the Foundation through their estate plan. If you have remembered NFCR in your estate, please call us at **1-800-321-CURE** and ask for Elizabeth Diamond.

Bequests

A donor may include a bequest to NFCR in a will. A bequest may be for a specific amount, a percentage of the donor's estate, or even a residual portion. Bequests help offset estate taxes and allow a donor to make a significant gift that might not have been possible during their lifetime.

Charitable Remainder Trust

Through a remainder gift, a donor may contribute assets such as securities or real estate to NFCR while retaining the income from those assets for themselves or a beneficiary. A remainder gift allows the donor to take an income tax charitable deduction for a portion of the value of the gift.

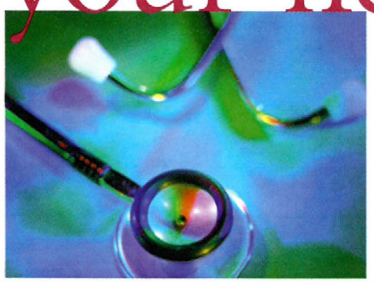
Charitable Gift Annuity

With a gift annuity, you make a contribution of cash, securities or other assets to NFCR. In return, NFCR agrees to make fixed payments to you and/or a beneficiary for life. A portion of your gift is tax-deductible depending on factors such as age and the amount of your contribution. In addition, a portion of the payments you receive from NFCR may provide tax benefits. For more information, call us at **1-800-321-CURE.**

Left: Csaba Horvath, Ph.D. (seated)

on your health






Cancer Detection

The cure rate for cancer is greatly increased by early discovery. Periodic health appraisals, screening tests and self-examination may save your life!

Your age, family medical history, lifestyle and occupation are important factors your doctor will consider. Please keep in mind your doctor may have good reason to do things differently based on your individual case.

[1] As a minimum, includes history, physical exam, blood/urine laboratory tests and chest x-ray as determined by your doctor.

[2] Follow your physician's advice.

[3] Proctosigmoidoscopy—colon/rectal exam.

[4] Those in high risk should begin at age 45.

The **On Your Health** series is presented as a public service by the National Foundation for **Cancer Research.** If you would like copies, call **1-800-321-CURE** or write NFCR, 4600 East West Highway, Suite 525, Bethesda, MD 20814.

Test or Procedure

Age	Frequency	Females	Males
18-20	One time Monthly Yearly	Complete Health Exam[1] Skin self-exam Pap smear[2]	Complete Health Exam[1] Skin self-exam Testis self-exam
20-40	Every 5 years Monthly Yearly	Complete Health Exam[1] Skin self-exam Breast self-exam Pelvic exam Pap smear[2]	Complete Health Exam[1] Skin self-exam Testis self-exam
40-50	Every 3 years Monthly Yearly Every 1-2 yrs.	Complete Health Exam[1] Skin self-exam Breast self-exam Pelvic exam Pap smear[2] Rectal exam Stool blood test Mammogram[2]	Complete Health Exam[1] Skin self-exam Testis self-exam Rectal exam Stool blood test
50-65	Every 2 yrs Monthly Yearly Every 3-5 yrs.	Complete Health Exam[1] Skin self-exam Breast self-exam Pelvic exam Pap smear[2] Rectal exam Stool blood test Mammogram[2] Procto[3]	Complete Health Exam[1] Skin self-exam Testis self-exam Rectal exam Stool blood test Prostate Specific Antigen Test[4] Procto[3]
65+	Every year Monthly Yearly Every 3-5 yrs.	Complete Health Exam[1] Skin self-exam Breast self-exam Pelvic exam Pap smear[2] Rectal exam Stool blood test Mammogram[2] Procto[3]	Complete Health Exam[1] Skin self-exam Testis self-exam Rectal exam Stool blood test Prostate Specific Antigen Test[4] Procto[3]

research for a cure
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