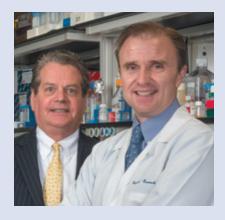


NFCR MISSION STATEMENT

The National Foundation for Cancer Research (NFCR) was founded in 1973 to support cancer research and public education relating to prevention, early diagnosis, better treatments and ultimately, a cure for cancer. NFCR promotes and facilitates collaboration among scientists to accelerate the pace of discovery from bench to bedside. NFCR is about Research for a Cure — cures for *all* types of cancer.

TABLE OF CONTENTS

Letter from the Chief Executive Officer
T-Cell Army
Targeting Cancer: Research Highlights4
International Collaboration Drives Discovery
2014 Szent-Györgyi Prize
2014 Fundraising Events
Play4TheCure
Extraordinary Support







RESEARCH CURES CANCER

Dear Friends and Donors,

For 42 years, the National Foundation for Cancer Research has funded scientific discoveries, medical advancements, and changes in technology that have revolutionized the way doctors treat cancer — all types of cancer. NFCR has long been a catalyst for the invention of the kinds of "disruptive innovations" that are bringing hope and promise to patients suffering with cancer.

Innovation is deeply embedded in all that we do. Our focus has always been to provide scientists the "adventure" funding to discover, and then to incubate their novel ideas, programs, products, or practices in support of research that will cure cancer. Since our founding by Nobel Laureate Dr. Albert Szent-Györgyi, NFCR has stood apart by supporting the High-Risk/High-Reward cancer research that larger charities and governments can't and won't fund.

But research is about more than just funding discoveries. There is a deafening silence about available cancer treatments today which needs to be addressed if we hope to translate the breakthroughs in research to patients at their bedsides.

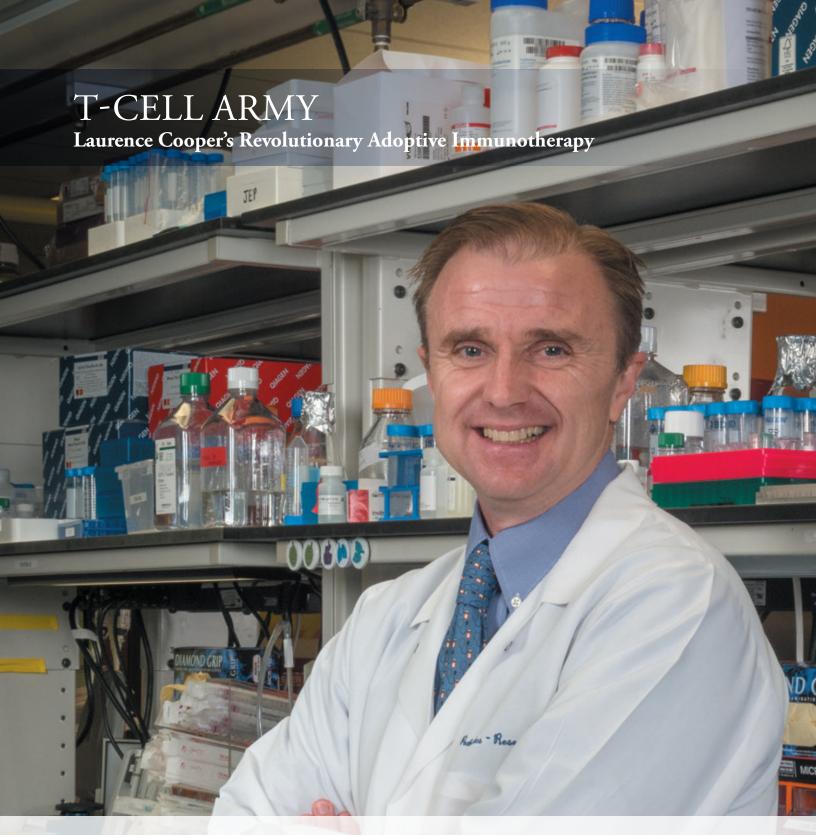
NFCR is dedicated to shortening the time between a laboratory discovery and a new treatment option becoming available to patients. The new breakthroughs and technologies our supported-scientists and international partners are working on are made possible by your generous support.

As you will see in detail in the following pages, NFCR supported-scientists are literally defining the forefront of cancer research. They are pioneering new approaches to immunotherapy, harnessing the immune system to fight cancer. They are also integrating molecular-based diagnostics with medical informatics to identify molecular targets in individual patients that might rapidly be translated into precision medicine strategies. This is *Research* for a **Cure**.

Thank you and sincerely,

Fanklingligburg

Franklin C. Salisbury, Jr. Chief Executive Officer



Sitting in his Houston, Texas laboratory, Laurence Cooper, M.D., Ph.D., is determined. "We've got to do better," he says. As a pediatric oncologist at MD Anderson Cancer Center, Dr. Cooper knows the cost of cancer first-hand. Despite great advances in the fight against childhood cancers, current treatments have reached the point of diminishing returns.

As a cancer researcher, however, Dr. Cooper also knows that the groundbreaking new treatments his patients desperately need will be found in the laboratory. NFCR shares this vision, and we have proudly supported Dr. Cooper's research efforts for over a decade. Today, thanks to his tireless work, a breakthrough new treatment called **adoptive immunotherapy** is now poised to reach patients across the country.

here are many different approaches to "immunotherapy," which refers to any treatment that harnesses the power of the immune system to fight cancer. Most approaches involve T-cells, an especially attractive part of the immune system for cancer research, for three reasons. First, T-cells are specific, which means they can recognize very subtle differences between normal and abnormal cells. Second, T-cells have memory, so that once they recognize a harmful molecular signature - whether due to a virus or to cancer - they can protect against recurrence for life. Third, T-cells are incredibly adaptable. Cancer researchers have long known that tumor cells can evolve resistance to drugs over time; unlike drugs, T-cells are able to evolve alongside the cancer and remain effective.

For decades, scientists have been trying to mobilize T-cells to identify and attack cancer cells. Through an ingenious process of genetic engineering, Dr. Cooper has now achieved remarkable success.

ASSEMBLING THE ARMY

When President Nixon declared "War on Cancer" in 1971, he was not referring to any specific treatment. However, Dr. Cooper believes it's an apt analogy for his approach to immunotherapy. "We do think of it as sort of a war metaphor," he says. "The T-cells can be thought of as foot soldiers, where they can be assembled outside of the body, just like a general would assemble an army."

Next the T-cells are "trained" to distinguish friend from foe - that is, to recognize tumor cells as different from normal cells - through a sophisticated process of genetic engineering. Dr. Cooper and his colleagues construct synthetic genes in the laboratory, which they insert into the genome of the assembled T-cells. These synthetic genes are designed to make the T-cells build special molecules, called chimeric antigen receptors (CARs), which act as "homing antennas" to direct the T-cells' killing abilities towards specific, pre-selected targets.

Now fully equipped to mount an attack against the cancer cells, the T-cells can be packaged, put into a bottle, and ultimately "deployed" back into the cancer patient's bloodstream. Importantly, Dr. Cooper's innovative genetic engineering approach also reduces the need to "match" donors with patients, allowing the T-cells prepared from a single, unrelated, healthy donor to be produced in bulk. These genetically engineered T-cells can be assembled and frozen in large quantities, like a "standing army reserve", then thawed and infused on demand when the patient needs them.

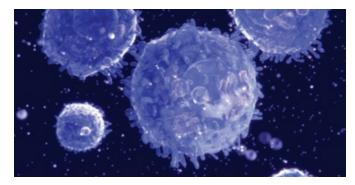
This revolutionary process, known as adoptive immunotherapy, is the culmination of years of work by Dr. Cooper, with support from NFCR.

FINDING THE FOES

Just as a good general trains an army to face the specific battles ahead, Dr. Cooper's pioneering approach can produce T-cells that are tailored to fight different types of cancer.

The first great success came with the engineering of CARs that enabled the T-cells to recognize a molecule called CD19, which is found on tumor cells from several types of leukemia and lymphoma. Dr. Cooper led the first-in-humans trial to infuse CD19-specific T-cells into patients with malignant B-cell Lymphoma.

Dr. Cooper has also generated CARs that grant T-cells specificity for other cancer molecules, including HERV-K, which is expressed



in certain types of breast cancer; CD56, which is expressed in the childhood cancer neuroblastoma; and c-Met, which is expressed in many different cancers, especially when tumors have a poor oxygen supply. As a result of this specificity and adaptability, Dr. Cooper's adoptive immunotherapy approach has the potential to make an impact across a huge array of cancer types.

Direct assaults on tumor cells are not the only way that Dr. Cooper's T-cell armies are helping cancer patients. Bone marrow transplant is an important component of therapy for many cancer patients, but during recovery they have dangerously weakened immune systems. This leaves them vulnerable to opportunistic infections, especially caused by Aspergillus, the most common fungal infection in immunecompromised patients. Healthy people breathe in small quantities of this common mold every day without problems, but for bone marrow transplant patients, infection is lethal in over 60% of cases.

Now Dr. Cooper and his team have successfully applied their adoptive immunotherapy technique to killing Aspergillus cells. They have engineered CARs that enable T-cells to recognize a sugar molecule on this fungus. This new approach of targeting sugar molecules could be used to target other dangerous pathogens as well.

WINNING THE WAR

Over the course of his research career, Dr. Cooper has never lost sight of the patients who are depending on him. These patients fuel his drive to "do better," and not settle for the diminishing returns of conventional therapies. Throughout our long relationship, NFCR has always had the highest confidence in Dr. Cooper's ability to bridge the gap between what cancer therapy is, and what it needs to be. "I have to think of things that really aren't available," says Dr. Cooper, "things that are new and untested. Quite frankly, this is where the NFCR shines, because it's able essentially to hold that uncertainty."

Today, thanks to the generous support of NFCR's donors, what was once an untested idea is now becoming a life-saving reality. Early in 2015, a new company, Ziopharm, was launched to translate Dr. Cooper's adoptive immunotherapy approach into new treatments for patients in clinics across the U.S. This is an excellent example of NFCR's unique and successful approach to funding cancer research. By providing long-term support for the most promising science, we ultimately make possible the truly groundbreaking discoveries that will have a huge impact in the lives of cancer patients.

It is because of those patients that Dr. Cooper remains determined. "We're not going to do something that's just iterative," he says; "we're going to do something that's transformative. We're actually going to cure – if I can use big words – we're going to cure cancer." That is the mission of NFCR: Research for a Cure.



For more than 40 years, NFCR has provided outstanding researchers with the precious seed funding they need to pursue the next big thing in cancer research. NFCR is committed to fostering scientific creativity, investing in basic research, and helping scientists translate these promising cancer discoveries into cures.

From life-saving breakthroughs in immunotherapy to advances in metastasis research, cancer genetics, precision medicine, anti-angiogenic therapies, nanomedicine and more, NFCR scientists have led the way into a new era of cancer prevention, detection, and treatment.

This is what NFCR means by Research for a Cure.

EARLY CANCER DETECTION AND MONITORING

Early detection and monitoring is critical for effective cancer treatments. The molecular differences that make cancer cells lethal also provide the clues for their detection, identification and visualization. Our scientists are developing new methods in molecular imaging technologies which are highly-sensitive cancer detectors. A revolutionary technology recently developed by NFCR-funded researchers makes it possible to detect early-stage cancer through a simple blood test. We envision that the development of these new tools for early cancer detection and continuous monitoring during and after cancer treatment will significantly improve clinical management of various cancers and ultimately, improve patient survival.

CTC CHIP DETECTS CANCER IN BLOOD



Daniel A. Haber, M.D., Ph.D. Massachusetts General Hospital, Boston, MA Supported Since: 2004 Principal Cancer Types: Pancreas, Breast, Lung, Melanoma, Prostate Research Focus: Circulating Tumor

Dr. Haber and his team developed the CTC iChip — an advanced micro-engineered device that is capable of capturing extremely rare circulating tumor cells (CTCs) from the blood. This device could dramatically improve treatment and diagnosis of many different types of metastatic cancer. Thanks to recent improvements in design, Dr. Haber is now able to use the CTC iChip to investigate the ways in which cancer cells leave the primary tumor and invade into the bloodstream to spread and initiate metastasis. By testing the CTCs, they have discovered that some genes are specifically activated as cancer cells leave the tumor and enter blood circulation. He and his team are now working to understand the properties of these genes to better understand how cancer cells spread through the blood, and whether targeting these genes could prevent metastasis.

MOLECULAR IMAGING



James Basilion, Ph.D. NFCR Center for Molecular Imaging, Case Western Reserve University, Cleveland, OH Supported Since: 2001 Principal Cancer Types: Breast, Brain, Skin Research Focus: Molecular Imaging of Cancer

Dr. Basilion and his team at the NFCR Center for Molecular Imaging are developing advanced new techniques that could literally change the way doctors look at cancer. Each tumor has a complex genetic signature, and a new molecular probe designed at the Center

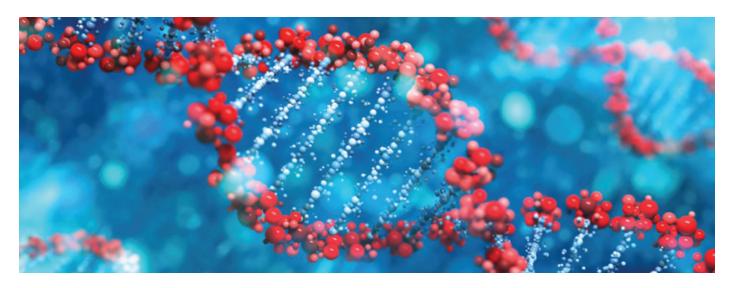
allows doctors to simultaneously visualize many different aspects of this signature in real-time — leading to better diagnostics. Dr. Basilion and scientists at the Center have also developed an imaging technique that could revolutionize cancer surgery, both for breast lumpectomy and skin cancer. The new technology consists of a light-emitting probe that binds to the cancers cells. It is many times more sensitive than existing probes and works within minutes, allowing surgeons to assess in real-time whether the margins of their surgeries are cancer-free. This novel approach, which may soon advance to clinical trials, could dramatically reduce the re-excision rates (currently 20-60% for lumpectomy), and more importantly reduce or eliminate local recurrence due to "surgically missed" cancerous tissues.

DETECTING OVARIAN CANCER



Robert C. Bast, Jr., M.D. MD Anderson Cancer Center, Houston, TX Supported Since: 2001 Principal Cancer Type: Ovarian Research Focus: Early Detection of Ovarian Cancer

When it comes to ovarian cancer, early detection is viewed as the most effective means to achieve cure. The five-year survival rate is above 90% if ovarian cancer is found during the earliest stage; unfortunately, only 15% of cases are diagnosed at this stage. Dr. Bast is working to change that. Using a special imaging device called a Superconducting Quantum Interfering Device (SQUID), which promises to improve sensitivity by several orders of magnitude over existing techniques, Dr. Bast and his colleagues are working to identify the best combination of biomarkers that can be used together to produce the most sensitive, ovarian-cancer-identifying signal possible. Using more specific and sensitive biomarkers in conjunction with SQUID technology could greatly increase early detection and diagnosis of ovarian tumors at a time that would offer the best opportunity for cure.



ADVANCING PERSONALIZED MEDICINE THROUGH ANALYSIS OF CANCER PATHWAYS AND DRUG RESISTANCE

What makes cancer cells different and dangerous? Among the myriad genetic alterations observed in tumors, only some propel cancer cells to proliferate abnormally, survive inappropriately and resist the drugs administered to destroy them. Furthermore, every cancer is different as multiple pathways can lead to the lethal growth of cancer. To know which alterations represent important therapeutic targets, we need to understand their place in the vast molecular network that underpins cellular function. We are using multiple genomic, proteomic, computational, and *in vivo* approaches to build a comprehensive "wiring diagram" for cancer cells and their molecular environment. This blueprint will lead us to better, more sophisticated strategies to control individual cancers and combat drug resistance.

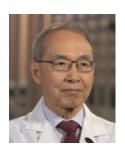
TARGETING GLIOBLASTOMA



Webster K. Cavenee, Ph.D.

Ludwig Institute for Cancer Research,
San Diego, CA
Supported Since: 2002
Principal Cancer Type: Brain (GBM)
Research Focus: New Therapies for
Brain Tumors

Dr. Cavenee is a renowned leader in identifying the genetic underpinnings of glioblastoma multiforme (GBM) — the most common and deadliest form of brain tumor — and creating innovative therapeutic approaches against this disease. He and his team are especially interested in understanding how GBM tumors become resistant to treatment. To date, the specific reasons that GBM develops resistance to new treatments (including a class of drugs called EGFR inhibitors) remain largely undefined. Dr. Cavenee's idea is that understanding this process will allow them to devise a way to block all of the resistance "escape pathways" using targeted therapies — an approach they believe will eventually lead to longer survival times for patients.



W. K. Alfred Yung, Ph.D.

MD Anderson Cancer Center,

Houston, TX

Supported Since: 2014

Principal Cancer Types: Brain

Research Focus: Overcoming Resistance
in GBM

In his first year of NFCR support, Dr. Yung is advancing the search for new treatments for glioblastoma multiforme (GBM) — the most common and deadliest brain tumor in adults. He is especially focused on drugs which target a gene called PI3K, a key driver for about 30% of GBM cases. Dr. Yung's team is working with a special panel of glioma stem cells (GSCs) collected from many different GBM patients, which allows them to investigate patterns of resistance to PI3K inhibitors. By establishing the molecular profile of each line of GSCs, Dr. Yung and his team can identify potential targets for new drugs in the laboratory, validate which targets are viable for treatment, and ultimately develop drugs that are specifically tailored to attack those targets.

STOPPING METASTASIS



Danny Welch, Ph.D. NFCR Center for Metastasis Research The University of Kansas Cancer Center, Kansas City, KS

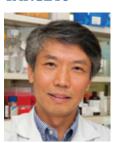
Supported Since: 1996

Principal Cancer Types: Breast, Colorectal, Lung, Ovarian, Pancreas, Prostate, Melanoma

Research Focus: Metastasis Suppressor Genes

Since its inception, Dr. Welch has directed the NFCR Center for Metastasis Research in its investigations of cancer biology related to metastasis — the process responsible for the vast majority of patient deaths across all types of cancer. Dr. Welch and his team have identified genes regulating metastasis, particularly metastasis suppressors; investigated the interactions between metastases and their surrounding tissues, especially for bone metastases; and are now working to translate their findings into clinical practice. In 2014, they identified genetic changes that predict whether patients will or will not develop metastasis. At least some of these changes occur in mitochondria — where cells convert nutrients into energy. These results could mean that a simple blood draw and analysis of mitochondrial DNA, which is present in every cell and which is small enough to be rapidly analyzed, could be used to help doctors guide their strategy to treat patients.

BIOMARKERS AND NEW THERAPEUTIC **TARGETS**



Wei Zhang, Ph.D. NFCR Center for Cancer Systems Informatics MD Anderson Cancer Center, Houston, TX Supported Since: 2006 Principal Cancer Types: Gastric, Ovarian, Uterine, Colorectal, Breast, Brain Research Focus: Cancer Genetics and Personalized Medicine

Personalized medicine — choosing anti-cancer treatments for specific patients based on the genetic makeup of their own, unique tumors — has been the dream of oncologists for decades. However, efficiently analyzing enormous genomic datasets to make treatment recommendations is no easy feat. Dr. Zhang and his team at the NFCR Center for Cancer Systems Informatics have the tools and the drive to make that dream a reality. With key publications in 2014 detailing discoveries in genomic and genetic makeup of ovarian and uterine cancer, plus their critical role in the international effort to map the genetic signatures of gastric cancer (page 13), investigators at the Center have accelerated the pace of research into this critical area, making invaluable contributions to our understanding of the molecular and genomic events that underlie many cancer types, and ultimately improving patient care.

ANTI-CANCER DRUG DESIGN AND DISCOVERY



Alanna Schepartz, Ph.D. Yale University, New Haven, CT Supported Since: 1991 Principal Cancer Types: Lung, Colorectal, Head and Neck, Pancreas Research Focus: Protein-Protein Interactions

Dr. Schepartz is pioneering a new approach to cancer treatment, which focuses on how to attack "protein-protein interactions" — one of the most challenging aspects of new drug development. In her laboratory, Dr. Schepartz and her team are synthesizing a new class of molecules called "miniature proteins" which they are using to identify the functional role of discrete protein-protein interactions that are critical for cancer. They are also developing beta-peptides — another class of synthetic molecule — that are able to block these interactions. In 2014, Dr. Schepartz described new molecules that inhibit EGFR — an important protein that is often mutated in lung cancer — in a new way, offering hope to patients whose cancer is resistant to current anti-EGFR treatments.



Alan C. Sartorelli, Ph.D. (1931-2015)Yale University School of Medicine, New Haven, CT Supported Since: 2004 Principal Cancer Types: Cervical, Ovarian, Breast, Brain, Leukemia Research Focus: New Drug Development

Dr. Sartorelli has been working for years to turn the tables on cancer, with an approach that converts the disease's apparent strength into a fatal weakness. Cancer often results when cells develop defects in their ability to repair damage to their DNA. This causes the cells to acquire even more mutations, which can ultimately lead to cancer. Dr. Sartorelli's team continues to work on identifying the specific flaws in DNA repair machinery in cancer cells, then attacking those cells with novel agents and/or chemotherapy that maximizes the specific type of DNA damage that they are unable to repair. Triapine, a novel agent of this type that was developed in Dr. Sartorelli's lab, is expected to enter clinical trials for the treatment of cervical and ovarian cancers in 2015. These approaches are also anticipated to have high relevance to the treatment of breast cancer, glioblastoma, and leukemia.



Paul Schimmel, Ph.D. Scripps Research Institute, San Diego, CA Supported Since: 1994 Principal Cancer Types: Melanoma, Leukemia Research Focus: New Avenues for Cancer Treatment

A world-renowned biochemist, Dr. Schimmel has dedicated his 40-year career to understanding the most fundamental chemical process for all living things — how the genetic information encoded in RNA gets translated into protein. His work has led to the discovery of a major new way to relieve the adverse effects of cancer drugs that can harm other parts of the body, especially the blood supply. One key protein Dr. Schimmel has been investigating was found to restore platelet counts, offering hope for cancer patients with thrombocytopenia. In addition, Dr. Schimmel and his team discovered how a natural ingredient in the food chain (resveratrol, found in cacao and grape skins) works with another key protein to produce protective effects against cancer — a true breakthrough for cancer prevention. The mechanism could also be exploited to develop new treatments or chemoprevention agents.

Daniel Von Hoff, M.D.



Laurence Hurley, Ph.D. NFCR Center for Targeted Cancer Therapies, Translational Genomics Research Institute, Phoenix, AZ Supported Since: 1985 Principal Cancer Types: Pancreas, Multiple Myeloma, Lymphoma, Colorectal Research Focus: New Drug Development



At the NFCR Center for Targeted Cancer Therapies, Co-Directors Dr. Von Hoff and Dr. Hurley are pioneering new approaches to attack the so-called "undruggable" targets present in many tumors. They have had great success identifying multiple new compounds that selectively kill pancreatic cancer cells with mutations in the K-ras

gene, and the leading compounds are currently being further developed for possible translation into the clinic. In addition to this, the Center is embarking on an entirely new approach to treating cancer in 2015, developing drugs that block newly-recognized genetic structures called "super enhancers." These large clusters of DNA regulatory elements, which control expression of a host of genes — including the critical cancer gene c-Myc — offer a great opportunity to disrupt the network of genes-associated cancer. This new approach may lead to great improvements in the treatment of pancreatic cancer, lymphoma, multiple myeloma, and colorectal cancer, and other cancers.

PERSONALIZED APPROACH FOR MORE EFFECTIVE TREATMENT



Kathryn B. Horwitz, Ph.D. University of Colorado, Denver, CO Supported Since: 1985 Principal Cancer Type: Breast Research Focus: Combination Therapy for Breast Cancer

A surprising number of ER+PR+ breast cancer patients — those whose cancers are positive for estrogen and progesterone receptors — are resistant to hormone therapy, and 30% or more see their tumor return after being "cancer-free" for years, even decades, following anti-hormone and chemotherapy treatments. Dr. Horwitz is working to understand why. Her research has found that luminal breast tumors, which account for 75% of all breast tumors, actually contain four different types of cancer cells, some of which are resistant to hormone therapy — as though the patient had four different kinds of breast cancer at once. Her team is working to isolate each of these four cell types, then find drugs that can attack each one, in hopes that combination therapy will prove to be a better long-term approach to treatment.



Waun Ki Hong, M.D. MD Anderson Cancer Center, Houston, TX Supported Since: 1999 Principal Cancer Type: Lung Research Focus: Adaptive Clinical Trials

Dr. Hong was instrumental in the design and implementation of the Biomarker-Integrated Approaches of Targeted Therapy for Lung Cancer Elimination (BATTLE) program, which was funded in part by NFCR. The BATTLE trial's adaptive design, in which lung cancer patients were assigned to be treated with the drug to which they are most likely to respond, based on their personal biomarker profile identified through tumor biopsies, was groundbreaking in its large-scale application of precision medicine techniques. Today, the BATTLE trial serves as a model for personalized treatment initiatives that are at the forefront of cancer research. Dr. Hong's work continues to pay dividends, as the trial's findings are applied in the clinic for lung patients with non-small cell lung cancer.

ANGIOGENESIS: SHUTTING DOWN CANCER



Harold F. Dvorak, M.D. Beth Israel Deaconess Medical Center, Boston, MA Supported Since: 1980

Principal Cancer Types: All Types (tumor blood supply)

Research Focus: Tumor Angiogenesis and Anti-vascular Therapy

Dr. Dvorak is a long-time NFCR Fellow, and winner of the inaugural Albert Szent-Györgyi Prize for his discovery of VEGF (vascular endothelial growth factor). VEGF plays a central role in angiogenesis, the process by which tumors recruit blood vessels to supply the nutrients they need to grow and survive. Dr. Dvorak's research has contributed immensely to scientists' understanding of this process, and led to the development of a new class of anti-angiogenic therapies that target tumor blood vessels. His latest work is focused on "feeding arteries" and "draining veins" — the larger vessels that carry blood into and out tumors — with the goal of determining how they form and whether they can be targeted to cut off the tumor blood supply. This novel approach, which is analogous to cutting off the water supply at the street, rather than turning off all the faucets in the house, has great potential for treating and possibly curing many types of cancer.



Rakesh K. Jain, Ph.D. Massachusetts General Hospital, Boston, MA Supported Since: 1998

Principal Cancer Types: Brain, All Types (tumor blood supply)

Research Focus: Attacking Brain Tumor Blood Vessels

Dr. Jain is a leader in the field of anti-angiogenic therapy. His seminal research demonstrated that anti-angiogenic therapy works by normalizing the abnormal, leaky vessels that usually surround and penetrate tumors — a process that both improves delivery of chemotherapy drugs and increases the oxygen content of cancer cells, which makes radiation therapy more effective. Dr. Jain is now focused on the role of angiogenesis in glioblastoma multiforme (GBM). By identifying the characteristics that confer resistance to anti-angiogenic therapy in patients with the disease, Dr. Jain's research is helping doctors to better tailor the use of anti-angiogenic therapies for GBM patients in the clinic. Additionally, the molecular resistance pathways that Dr. Jain and his team identify will direct the development of novel agents targeting these pathways, which could extend the benefits of anti-angiogenic therapy for patients.

OVERCOMING DRUG RESISTANCE



Susan Band Horwitz, Ph.D. Albert Einstein College of Medicine, New York, NY Supported Since: 2001 Principal Cancer Type: Breast, Ovarian Research Focus: New Drug Development

Dr. Horwitz is a world-renowned cancer researcher, whose work has been instrumental in the development of a successful class of anti-cancer drugs called Microtubule-Stabilizing Agents (MSAs) a class that includes Taxol, Ixempra and others under development. However, oncologists find it difficult to know if a specific tumor will respond to one of these drugs. Because all cancer drugs have some toxic side effects, physicians only want to expose patients to a drug if it will have positive value. Dr. Horwitz and her team are working to understand the mechanisms of action of drugs affecting the tubulin/microtubule system, and to find biomarkers that will help doctors know which patients will benefit from which drugs. By understanding the mechanisms of cell death, Dr. Horwitz should be better able to select new drugs and design combinations of drugs that will destroy cancer cells.



Alice Shaw, M.D., Ph.D. Massachusetts General Hospital, Boston, MA Supported Since: 2014 Principal Cancer Types: Lung Research Focus: Overcoming Drug Resistance

Joining NFCR this year with the support of the Hillsberg Lung Cancer Translational Research Grant, Dr. Shaw got right to work, publishing a breakthrough article in the journal Science about a new platform she and her team developed to rapidly identify effective drug combinations for lung cancer patients whose tumors have stopped responding to targeted therapy. In their research, cells taken directly from patients' tumors were grown in the laboratory and treated with a host of different drug combinations to find the ones that work — both attacking the cancer, and cutting off the "escape pathways" that can cause resistance. The approach identified several effective drug combinations — including some that standard testing would not have predicted to work. With further refinements, this strategy might be used to select the optimal treatment for each individual patient, making precision medicine a reality for lung cancer patients — and for other types of cancer as well.



Jin Jen, M.D., Ph.D. Mayo Clinic, Rochester, MN Supported Since: 2014 Principal Cancer Types: Lung Research Focus: Personalized Medicine

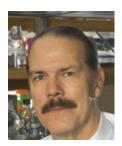
Dr. Jen and her team are developing a platform for rapid selection of personalized treatment options for individual lung cancer patients. In an exciting project supported through the Hillsberg Lung Cancer Translational Research Grant, Dr. Jen is performing advanced genomic analysis on tumor biopsies collected from lung cancer patients whose cancer has recurred, to identify drugs that can target the specific genetic mutations driving the patient's cancer. Meanwhile she has also established tumor models derived from the same patients' biopsies. By integrating the genetic, clinical, and patient-specific tumor model data, Dr. Jen's research will help doctors choose the best possible drug for each specific patient in the project, which will potentially demonstrate the validity of a direct approach to personalized medicine.

INNOVATIVE THERAPIES



Wayne Marasco, M.D., Ph.D. NFCR Center for Therapeutic Antibody Engineering, Dana-Farber Cancer Institute, Harvard Medical School. Boston, MA Supported Since: 1994 Principal Cancer Types: Kidney, Head and Neck, Lung Research Focus: Monoclonal Antibody Therapy

One promising approach to treating cancer is monoclonal antibody therapy — a type of immunotherapy in which specialized proteins called antibodies attach to specific structures on the surface of cancer cells, then alert the patient's own immune cells to attack the cancer. Designing the antibodies for this type of therapy is a challenging feat of molecular engineering — one ably met by Dr. Marasco and his team at the NFCR Center for Therapeutic Antibody Engineering. Dr. Marasco has had great success developing antibodies that attach to carbonic anhydrase IX (CAIX), an important protein expressed in renal cell carcinoma — the most common type of kidney cancer and recently reported in cancers of the mouth and lungs as well. For Dr. Marasco, the ultimate goal is always to translate his findings into new drugs for patients, and in 2015 he hopes to move his anti-CAIX antibodies into clinical trials.



Paul B. Fisher, M.Ph., Ph.D. Virginia Commonwealth University School of Medicine, Richmond, VA Supported Since: 2008 Principal Cancer Types: Prostate, Pancreas, Metastatic Bone Cancer Research Focus: Cancer Terminator Viruses

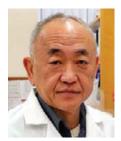
Dr. Fisher has developed a new therapeutic approach to cancer therapy, which he calls a Cancer Terminator Virus. The agent, which is a virus genetically reprogrammed to infect and destroy tumor cells while leaving normal cells alone, is used to treat both early stage and metastatic prostate cancer, and recently expanded to treatment of pancreatic cancer as well. Dr. Fisher has also developed the first sensitive and specific imaging agent for bone metastases — the number one cause of death for patients with prostate cancer. The new molecular imaging technique detects cells that express a gene called AEG-1, which was originally discovered by Dr. Fisher. It is expressed at high levels in all cancer types investigated so far, with limited expression in normal tissue. This represents a great improvement over current clinical imaging techniques, and could lead to earlier detection and treatment of metastases — not only originating from prostate cancer, but from several other cancer types as well.



Curt Civin, M.D. University of Maryland School of Medicine, Baltimore, MD Supported Since: 1997 Principal Cancer Types: Leukemia Research Focus: Advancing Artemisinins for AML Treatment

Leukemia is a great success story for cancer research — one in which Dr. Civin played an important role. His early work on bone marrow stem cell transplantation was partially responsible for the dramatic increase in 5-year survival for all types of leukemia over the past 20 years. Unfortunately, acute myeloid leukemia (AML) remains the deadliest form of leukemia. Dr. Civin discovered that artemisinins, a class of drugs used to treat malaria, are also effective at killing AML cancer cells. In 2014, he identified ART-838, a specific artemisinin compound that shows remarkable preliminary effectiveness against leukemia cells, works well in combination with established anti-leukemia drugs, can be given orally and stays active in the bloodstream for a long time, and doesn't appear to harm normal bone marrow cells. ART-838 may prove to be an effective new treatment for AML patients.

CHINESE HERBAL MEDICINE: ADJUVANT TO CHEMO AND RADIATION THERAPY



Yung-Chi Cheng, Ph.D. Yale University School of Medicine, New Haven, CT Supported Since: 1991 Principal Cancer Types: Pancreas, Colorectal, Liver, Lung Research Focus: Traditional Chinese Medicine

While the therapeutic effects of Traditional

Chinese Medicine (TCM) have been documented anecdotally for centuries, they have been too often discounted by modern medicine as "alternative therapy" because there was little rigorous scientific proof of their effectiveness. Dr. Cheng's laboratory is working to bring TCM into the mainstream of western medicine. Their formulation of an ancient Chinese herbal formula, PHY906, is currently being evaluated in two separate Phase 2 clinical trials as an adjunct to the chemotherapy agent irrinotecan (Camptosar®) for colorectal cancer patients, and in combination with the drug Sorafenib in patients with liver cancer. PHY906 could become one of the first FDA-approved oral herbal medicines for cancer treatment. Dr. Cheng and his team are also evaluating other herbal

DEVELOPING NANOTECHNOLOGY-BASED **CANCER THERAPIES**

formulas from TCM, with the hope of developing a new class of

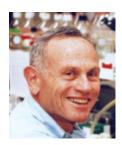


anti-cancer drugs.

Esther H. Chang, Ph.D. Georgetown University, Washington, D.C. Supported Since: 1988 Principal Cancer Type: Ovarian, Breast, Brain, and Childhood Cancer Research Focus: Nanomedicine

Dr. Chang has developed a new platform for treating cancer that is currently being advanced in three separate Phase 2 clinical trials. The platform involves three parts: 1) a nanoscale capsule that can travel through even the tiniest blood vessels, 2) a molecular targeting system that guides the capsule not only to the primary tumor, but to even the smallest metastases, and 3) a "payload" that the capsule delivers to the interior of the cancer cells. That payload can be any kind of anti-cancer agent, from conventional chemotherapy to the latest gene therapies — whatever can be enclosed in the capsule. In these Phase 2 trials, the payload is p53, a critical gene that normal cells have in abundance — making it essentially non-toxic — but which is missing in cancer cells. In Phase 1 trials, restoring p53 proved deadly to cancer cells.

CANCER PREVENTION



Michael B. Sporn, M.D. Dartmouth Medical School, Hanover, NH Supported Since: 1999 Principal Cancer Types: Pancreas, Breast, Lung Research Focus: Chemoprevention of Cancer

The best way to reduce the number of patients dying from cancer is to prevent the disease from developing in the first place. That is the goal of Dr. Sporn, who is establishing new approaches for the prevention and treatment of cancer. His research has led to the development of several synthetic triterpenoid compounds, a new class of chemical agents with potent preventative effects against several types of cancer, including breast, lung, and pancreatic cancer. For individuals who have a family history or are otherwise at high risk to develop these diseases, the promising results of Dr. Sporn's research offer hope that their chances of developing this devastating cancer may be dramatically reduced by the use of chemoprevention.



Helmut Sies, M.D. Heinrich-Heine-Universität, Düsseldorf, Germany Supported Since: 1983 Principal Cancer Types: Colorectal, Skin, Prostate Research Focus: Nutrition and Cancer Prevention, Implication of Micronutrients

Dr. Sies previously discovered that the antioxidant lycopene, a micronutrient found in tomatoes and other foods, has strong skin cancer prevention effects. Today, his research is focused on selenium (Se), a trace metal found in certain nuts and essential for good health. There is epidemiological evidence that adequate intake of selenium is beneficial for human health and cancer prevention especially colon cancer — and Dr. Sies is establishing the molecular basis for this effect. Key antioxidant enzymes called selenoproteins require selenium to repair oxidative damage. Dr. Sies discovered that not only are selenoproteins strongly decreased in colon cancer tumor cells, but they are strongly expressed by immune cells in the gut. Moreover, dietary selenium compounds were found to stimulate colon cells to produce selenoproteins, suggesting a potential mechanism for how selenium from ingested food supports immune health and cancer prevention.



In the four decades since NFCR's founding, we have made amazing progress in the fight against cancer, achieving breakthroughs in prevention, early detection, and treatment. Throughout this history there are two things we have learned: 1) Cancer is an incredibly complex disease, and the road to developing cures is long. 2) The journey is much faster and much easier if you aren't walking the road alone.

hen you are working to find a cure for cancer, simply being a brilliant research scientist is not enough. No one working in isolation can hope to unravel the complexities of cancer, much less translate their discoveries into benefits that patients desperately need.

To truly have an impact in the fight against cancer, we need to bring people together. Instead of building barriers to divide researchers, we are focused on building bridges — fostering relationships between scientists around the world and promoting collaborative efforts to fight cancer.

This approach has already produced results with direct impact on the lives of patients with gastric cancer, the fourth most common cancer and the second leading cause of cancer death in the world. In 2013, NFCR launched the new Center for Cancer Systems Informatics at MD Anderson Cancer Center, and last year we reported on their inaugural project: The Geographic Mapping of Gastric Cancer **Genomes.** In 2014, the project proved a stunning success, providing new genetic insights that could change the way oncologists treat this terrible disease. The results were published in the January 12, 2015 issue of the Proceedings of the National Academy of Science.

This was a truly collaborative research effort, with important contributions from NFCR Fellow Dr. Webster Cavenee, Director of the NFCR Center for Cancer Systems Informatics; Dr. Wei Zhang, and President of the Chinese Anti-Cancer Association and Director of the Tianjin Medical University Cancer Institute; Dr. Xishan Hao; and a team of scientists representing a dozen institutions globally.

Investigators used advanced genome-sequencing technology to analyze hundreds of gastric cancer tissue samples. They discovered that defects in three cellular signaling pathways (BRCA2, Wnt and PI3-K-ERBB4) might influence the response of gastric cancers to therapy.

This is very good news for gastric cancer patients, because a number of newly developed drugs are currently available which target these pathways. These drugs have already been tested in other cancer types, such as breast and ovarian cancers, suggesting that patients with gastric cancer may now be designated for the particular therapy indicated by their genetics. This approach, called "personalized medicine," could prove to be a major improvement over the current standard treatment for gastric cancer patients, which is essentially "one-size-fits-all."

The rise of personalized medicine confirms what NFCR has always believed — that the fastest way to end this disease is to research all types of cancer. In the same way that divisions between researchers at different institutions can slow the pace of discovery, when we enforce hard divisions between researchers working on different cancer "types", we run the risk of missing important areas of overlap.

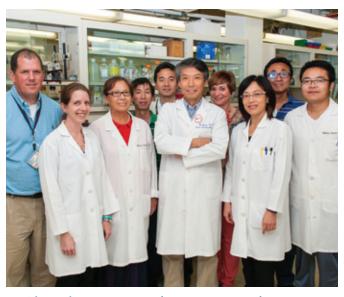
The success of the gastric cancer genomics project is the culmination of nearly a decade of NFCR support, as it was funded as part of our Tissue Bank Consortium in Asia (TBCA) — a collaborative platform that we established in 2004 to promote and facilitate biospecimen-based international cancer research. TBCA was made possible by grants from several global pharmaceutical companies, specifically in support of international collaboration. It is governed by an International Executive Steering Committee, chaired by NFCR

Fellow Dr. Webster Cavenee and composed of leading scientists from top research institutions, cancer hospitals, and industry in the United States and China. It operates in total compliance with the highest international standards for biospecimen collection, storage, and annotation. With TBCA, NFCR has established a new model for public-private partnership and academia-industry collaboration in cancer research across geographic boundaries.

NFCR is poised to continue this tradition of high-impact international collaboration in 2015 as well. In addition to our ongoing efforts against gastric cancer, NFCR has joined with the National Biomarker Development Alliance, the Cure Brain Cancer Foundation, and the National Brain Tumor Society to found The Global Brain Cancer Alliance. Together we have assembled a worldclass team to defeat glioblastoma (GBM), the deadliest form of brain cancer. For GBM patients, the need for new treatment options is tremendous. Because no effective long-term therapies are available, 90% of GBM patients survive less than 5 years after diagnosis, and over half of patients survive less than 15 months.

The scale of this global effort to defeat GBM is unprecedented, with over 150 participants from more than 40 leading cancer institutions, including Arizona State University, MD Anderson Cancer Center, Memorial Sloan Kettering, Dana Farber, and the Ludwig Institute. Under the leadership of the Executive Committee, chaired by Dr. Anna Barker and including NFCR President Dr. Sujuan Ba, longtime NFCR researcher Dr. Webster Cavenee, and NFCR Fellow Dr. W.K. Alfred Yung, a revolutionary new framework for GBM clinical trials is emerging. The goal is to allow GBM patients to quickly share in the benefits of more effective therapies, providing new hope where little currently exists.

Cancer knows no boundaries. It strikes people of all ages, from infants to the elderly, making no distinctions for gender, ethnicity, nationality, or religion. Cancer is a global problem, and it requires a global solution. That is why NFCR is committed to a program of international collaboration, in support of our mission: Research for a Cure.



Wei Zhang, Ph.D., NFCR Center for Cancer Systems Informatics, MD Anderson cancer Center with his team of scientists.

SZENT-GYÖRGYI PRIZE DR PROGRESS IN CANCER RESEARC



In recognition for his pioneering work in the area of cancer immunotherapy, Dr. James Allison was awarded the 2014 Szent-Györgyi Prize for Progress in Cancer Research. Dr. Allison's research led to the successful development of "immune checkpoint therapy," and the first FDA-approved drug for the treatment of metastatic melanoma. The Prize was presented at a ceremony in Washington, D.C., on April 30, 2014, at The National Press Club. U.S. Senator Jerry Moran (R–KS) delivered the keynote address, in which he praised Dr. Allison's accomplishments and stressed the need for increased funding of scientific research in general and cancer research in particular.

2014 SZENT-GYÖRGYI PRIZE

A Giant of Immunotherapy Receives NFCR's Most Prestigious Award

While mainstream cancer research and treatment focused for decades on radiation therapy and chemotherapy, Dr. Allison's trailblazing work in immunotherapy — working with the body's own immune system to fight off cancer — never ceased. Thanks to his extraordinary leadership, we have entered a new era in the treatment of cancer.

"Dr. Allison's work has already saved numerous lives and shines a bright light on a future direction of oncology," said Dr. Alex Matter, CEO of Experimental Therapeutics Centre & D3, A*STAR, Singapore, winner of the 2013 Szent-Györgyi Prize and Chair of this year's Prize Selection Committee. "He has validated the immunotherapy approach and turned previously widely-held beliefs on their heads with his discoveries. His work is extremely significant and constitutes a turning point in the history of progress in cancer treatments."

Dr. Allison, along with Dr. Jeff Bluestone, was the first to show that T-cells, the enforcers of the immune system, contain a protein receptor called CTLA-4, which acts as a checkpoint to shut down the immune response. Dr. Allison developed an antibody to block CTLA-4, which he hoped would unleash the immune system to attack cancer. After conducting extensive preclinical work, Dr. Allison showed that blockade of CTLA-4 did indeed lead to rejection of many types of tumors. This research led to the development of a drug called ipilimumab, the first drug to significantly extend survival for patients with late-stage melanoma. The FDA approved ipilimumab for treatment of metastatic melanoma in 2011, and it is now in clinical trials to treat a variety of other cancers.

"I am honored to receive this distinguished award from the National Foundation for Cancer Research for my work in immunology," said Dr. Allison. "It has been an encouraging journey thus far, and I am humbled to share this prize with the previous winners. The most important reward, however, has been the number of lives being saved using anti-CTLA-4 treatment and the prospect of more to come as checkpoint blockade develops as a major therapeutic approach to cancer."

"Dr. Allison has revolutionized the way science approaches cancer treatments. He is on the front line in the war against cancer and could not be more deserving of this award," said Sujuan Ba, Ph.D.,



2014 Szent-Györgyi Prize recipient James P. Allison, Ph.D.



Keynote Speaker Senator Jerry Moran (R-KS)

Co-chair of the 2014 Szent-Györgyi Prize Selection Committee and Chief Operating Officer of NFCR.

The Szent-Györgyi Prize honors a scientist for a seminal discovery that has resulted in a breakthrough in cancer research. The prize is awarded annually to a scientist, nominated by colleagues or peers, who has contributed outstanding, significant research to the fight against cancer, and whose accomplishments have helped improve treatment options for cancer patients. The prize is named in honor of NFCR co-founder Albert Szent-Györgyi, M.D., Ph.D., who won the Nobel Prize for Science and Medicine in 1937 for his discovery of Vitamin C.

ABOUT JAMES ALLISON, PH.D.

Dr. James Allison is currently the Chairman of the Immunology Department and executive director of the immunotherapy platform for the Moon Shots Program at UT MD Anderson Cancer Center in Houston. From 2004 to 2012, he served as Chairman of the Immunology Program and other distinguished positions at Memorial Sloan Kettering Cancer Center in New York. Prior to 2004, Dr. Allison was on the faculty of the University of California, Berkeley; Stanford University; and the University of Texas MD Anderson Cancer Center. He earned his Ph.D. in biological sciences from the University of Texas at Austin.

Dr. Allison is a member of the National Academy of Sciences, the Institute of Medicine of the National Academies, and a Howard Hughes Medical Institute alumnus. He has won numerous honors for biomedical research including the inaugural AACR-CRI Lloyd J. Old Award in Cancer Immunology, *The Economist's* 2013 Innovations Award for Bioscience, and a 2014 Breakthrough Prize in Life Sciences. He co-leads a Stand Up to Cancer Dream Team research project in immunotherapy.



Donor-initiated and corporate-sponsored special events are great ways to show support for cancer research and turn a passion to cure this disease into action. These events and programs help raise funds and awareness while also serving as a catalyst for many supporters of cancer research and prevention education to collaborate, expand their knowledge, and increase their commitment to helping NFCR find cures for all types of cancer.

The Lucy Fund



Tracy McAllister and Theresa Nussbaum share a smile at the 7th Annual Party4Life.

The Lucy Fund is dedicated to raising funds to support metastatic cancer research. In 2014, The Lucy Fund committee, along with the help of generous sponsors and many hard-working volunteers, hosted several events to raise awareness and funds to support metastatic cancer research.

The Lucy Fund held the 7th Annual Party4Life event in Brodheadsville, Pennsylvania. They also hosted the 2nd annual Party4Life event at Susquehanna University and an inaugural event at Misericordia University. The 2nd Annual Lucy Fund 5k took place in Cape Elizabeth, Maine. The inaugural Battle on Broad dance crew competition took place in December at Temple University. All events offered memorable ways to honor cancer survivors, give encouragement to those currently battling cancer, and remember those who have been lost.

The Lucy fund has raised over \$260,000 since its inception to support Dr. Danny Welch at the NFCR Center for Metastasis Research. Dr. Welch and his team have discovered six genes that suppress the spread of cancer. Right now, they are working on understanding the mechanism that governs how these genes work and more importantly, considering ways that these discoveries can be rapidly translated into new targeted therapies for patients whose cancer has spread.

Golf and Tennis Classic

The Annual Golf and Tennis Classic was held at Bethesda Country Club in Bethesda, Maryland on Monday, September 22, 2014. This was the 11th year for the Golf Classic and the inaugural year for the Tennis Classic. The event brought golfers and tennis players from across the country together for a terrific day on the course and courts to support a great cause.

The event raised over \$60,000 to support NFCR's life-saving cancer research programs. This year's event was sponsored by The Calmark Group with other significant sponsorships from Sports Chevrolet, Hendall Inc., PhRMA, Atlas Wood Floors, Inc., Enterprise Holdings, The US Oncology Network, iCore Networks, Inc., Copilevitz & Canter, LLC, QGA Public Affairs, Sage Title Group, WJE, and Long and Foster, Inc.

"We are so grateful to our sponsors, and for the volunteers who donated their time and energy to organize this event," said Tracy Tkac, Event Chair of the Golf and Tennis Classic. "We couldn't have done it without them, and as a result of their contributions we were able to raise thousands of dollars to support NFCR's innovative cancer research."



Tennis player Elizabeth Fratt and Golfer Bill Steele.

Daffodils and Diamonds



Attendees enjoying the event.

The 33rd Annual Daffodils and Diamonds Luncheon and Fashion Show took place on March 13, 2014, at Columbia Country Club in Chevy Chase, Maryland. The event has become a spring ritual, drawing hundreds of dedicated Washingtonian women each year. To date, it has raised over \$800,000 to support NFCR breast and ovarian cancer research programs. "This longstanding annual event is unique because it is held by women for women," said Lynn Novelli, Event Chair of the luncheon. "NFCR is making great strides in the field of cancer research, and this event gives us the opportunity to pour more resources into the cancers that specifically affect women."

This year's event was emceed by Alison Starling, WJLA TV ABC 7 News Anchor, with fashion show presented by Polly Sturm featuring fashions from ETCETERA Designer Separates Spring-Summer 2014 Collection. "The commitment of the volunteers and the generosity of our community made this event very successful, and we are proud to have been a part of it," said Polly Sturm, Committee Member.

The program also included a champagne reception and the presentation of several live and silent auction items, including a one-week stay in Copper Mountain, Colorado, a Judith Ripka White Sapphire Pendant and a beautiful Tory Burch bag.

PLAY4THECURE

Powering Cancer Research Through Teamwork



2014 saw the continued growth of NFCR's *Play4TheCure* sports fundraising program. Over 600 teams in 35 states answered the question, "Who Do You Play4?" *Play4TheCure* continues to inspire young athletes and their teams to use their passion for sports to "Play4" loved ones affected by cancer. NFCR encourages them to actively participate to fund cancer research and make a difference. The program has received support from a broad range of athletes, including youth recreation leagues, club teams, and high school and college teams across the country.



ne major achievement in 2014 was that NFCR was named the official charity of the National Field Hockey Coaches Association (NFHCA). This partnership solidified *Play4TheCure* as part of the fabric of the field hockey community. "The NFHCA is excited to partner with *Play4TheCure* to provide our members with the resources they need to motivate their communities to fundraise for cancer research. Teams have an opportunity to be a part of the impressive *Play4TheCure* brand, which goes beyond sports and shows our coaches and their players the power of giving back," said Andy Whitcomb, President of NFHCA.

NFCR also named Tina Reichprecht as an official advisor to the *Play4TheCure* program. Among her many notable achievements, Tina is the founder of *Play4TheCure* and the Mystix Field Hockey Club, and Board member of USA Field Hockey. NFCR is grateful for her passionate efforts to grow *Play4TheCure*. NFCR is also grateful to all the corporate supporters of *Play4TheCure*, especially Longstreth Sporting Goods for their continued generosity.

Play4TheCure continued to expand beyond field hockey with the addition of more games in soccer, lacrosse, and softball. We are proud of long-time member of the NFCR Board of Directors, Mark R. Baran, who organized his own personal Play4TheCure event. He joined other endurance swimmers in a two-mile open water race at Sunset Lake in Wildwood Crest, N.J., raising over \$9,000.





NFCR is excited about 2015, as more and more teams join the fight against cancer. We are honored to have such a loyal and committed group of coaches, players, and families who support NFCR through their dedication. "Having these girls a part of NFCR's *Play4TheCure* means so much to all of us," said Mo Minicus, head field hockey coach at Darien (CT) High School. "It's inspiring to hear the athletes tell us who they Play4, such as "my mom's a cancer survivor and I Play4TheCure". Every fundraiser makes a difference to help in the fight against cancer and NFCR looks forward to seeing even more participants as the program grows.

EXTRAORDINARY SUPPORT

2014 was distinguished by the extraordinary breadth and depth of support for NFCR. An unprecedented number of donors, corporations, foundations and institutions made gifts totaling \$15,350,000. We are deeply grateful to all of our donors for their generosity and confidence in our vision of *Research* for a Cure. Every gift, large and small, is an investment in new and better ways to prevent, diagnose and treat cancer. NFCR is about cancer research, for research will cure cancer.

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