2023 RESEARCH PROGRESS REPORT

NFCR™ | National Foundation for Cancer Research

We Make Cures Possible

50 YEARS OF DISCOVERY ... AND PROGRESS.

One mission. One unwaivering commitment.

To support pioneering cancer research in our quest to make cures possible.

Through the support of our donors and partners, NFCR is making an impact in the fight against cancer. Over the past 50 years, NFCR funded research has contributed to many breakthroughs in cancer early detection, prevention, and treatment.

We have momentum. We must maintain our focus. There are still many areas of unmet needs in cancer research. We must continue to raise the funds needed to support critical research programs that are showing promise and results toward our shared end goal. A world where cancer is a disease which has been cured.

With your help. This goal can become a reality.

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WITH YOUR CONTINUED SUPPORT – WE CAN MAKE CURES POSSIBLE.

We are pleased to share our 2023 Research Progress Report, highlighting examples of how our research funding has worked to save lives and what we are doing now to advance progress every day to defeat cancer.

Throughout our history, NFCR has played an impactful role, and our research programs have helped pave the way for progress in new detection, diagnosis, treatment, and prevention approaches for cancer patients. We have provided critically needed funding to some of the most influential scientists and breakthrough discoveries that have advanced cancer research.

NFCR is a unique charity in many ways. One of the most essential aspects of this organization is the community and network we have helped to build. NFCR is recognized for its unique spirit and ability to collaborate with all parts of cancer research, oncology, and patient care ecosystems. This sense of teamwork between key experts and thought leaders enables NFCR to ensure that the best and most innovative approaches to curing cancer are at our forefront.

Your past loyal support has enabled NFCR and our funded scientists to make an impact to cancer research and cancer patients. Your continued support of NFCR is critical–Much more must be done! With your continued support, we can address the unmet needs in cancer research to help provide new hope for cancer patients. More resources are needed to expand our research programs, especially early detection and early intervention. The discoveries of past investments are leading the way for how patients are treated today. The investment today will lead the way for better treatments for our children and grandchildren tomorrow.

We are all part of the cure, and when we work together, great things are possible.

Sincerely,

Sujuan Ba, Ph.D.
President and CEO, NFCR

50 YEARS OF DISCOVERY

UNWAVERING COMMITMENT TO PIONEERING CANCER RESEARCH.

Over the past 50 years, the National Foundation for Cancer Research has provided vital funding to make game-changing discoveries in cancer treatments, detection, prevention and, ultimately, a cure. NFCR has distinguished itself in the cancer research sector by emphasizing wholistic, long-term, transformative research often overlooked by other major funding sources — research that aims to cure all types of cancer. NFCR's unwavering commitment to this vision has yielded remarkable achievements and catalyzed groundbreaking discoveries that have transformed cancer treatment paradigms, providing new options for patients.

> **The whole point of basic research was to venture out into the unknown.**
>
> DR. ALBERT SZENT-GYÖRGYI

TUMOR ANGIOGENESIS

NFCR's impact is seen in Dr. Harold F. Dvorak's research on vascular endothelial growth factor (VEGF). When Dr. Dvorak discovered this molecule, he faced funding challenges for further studies. Franklin Salisbury's offer of support in 1980 proved pivotal. This support ultimately led to the identification of VEGF as a protein crucial for blood vessel formation in tumors, laying the foundation for anti-angiogenesis therapies and revolutionizing cancer treatment. NFCR's steadfast support has been instrumental in unraveling the complexities of tumor angiogenesis for over three decades. By delving into the mechanisms governing blood vessel formation in tumors, NFCR-backed scientists have significantly enhanced our comprehension of the tumor microenvironment. With this discovery, Avastin (bevacizumab) and several other medications were developed and approved by the FDA to treat colorectal, breast, lung, and various cancers, saving millions of lives.

GBM-AGILE

In the battle against glioblastoma (GBM), a devastating brain cancer, collaborative efforts from 150 global pioneers across 40 institutions, including Dr. Sujuan Ba, CEO of the National Foundation for Cancer Research, have worked together to launch the Glioblastoma Adaptive Global Innovation Learning Environment (GBM AGILE). Conceived in 2003, this initiative led by Drs. Anna Barker, Webster Cavenee, and W.K. Alfred Yung aimed to elevate GBM patient survival rates significantly. NFCR's integral role in GBM AGILE aligns with our commitment to impactful collaborative research. As a strategic supporter, NFCR, provided the critically needed seed grants to the initiative from the inception of the program and continues to support Global Coalition for Adaptive Research, the official sponsor for GBM AGILE. GBM AGILE pioneers a paradigm-shifting clinical trial approach, revolutionizing GBM therapy's evaluation. Unlike traditional trials, it concurrently assesses multiple drugs, utilizing

THE POWER OF YOUR DONATION

$25-$100

Stains one tissue slide from a tumor biopsy to look for a predictive biomarker of cancer metastasis

$100

Performs one biopsy to get tumor tissues from a patient for a variety of pathological tests and biological analyses

$250

Buys one case of petri dishes for growing cancer cells – an essential first step to identify tumor markers or test treatment effectiveness of new drugs

$500-750

Buys one antibody test to determine whether tumor cells have a specific marker for drug resistance

$1,000

Carries out a comprehensive genome-wide analysis on all genes in one tumor sample, for developing targeted and personalized cancer therapies

real-time data for dynamic adjustments for patients. This groundbreaking design accelerates drug development, offering newfound hope for GBM patients. Since GBM AGILE was open to recruit patients July 2019 launch, it has screened over 1,500 patients and included six investigational drugs. The impact of GBM AGILE promises transformative strides in GBM treatment – providing new hope to cancer patients.

GBM AGILE
Adaptive Global Innovative Learning Environment

Targeted Therapies and Personalized Medicine

NFCR's pivotal contributions have advanced the identification of critical oncogenes and tumor suppressor genes, providing the foundational knowledge for targeted therapies and personalized medicine approaches. This area of impact has redefined the way cancer is treated, offering more precise and effective solutions.

Genomoics and Proteomics

Recognizing early the potential of genomics and proteomics in cancer research, NFCR has played a crucial role in enabling scientists to explore the genetic and proteomic landscape of cancer. This area of impact has unearthed novel therapeutic targets, paving the way for innovative treatment modalities.

We have never wavered from our original vision. We've made 50 years of progress, and now we need people to help us fund the breakthroughs of the next 50 years. Today, we have the infrastructure, the network, the power and the knowledge needed. We're moving full steam ahead, seeding new ideas and exploringnew frontiers for future discoveries, all while pushing those discoveries into clinical trials. With the help of our donors, we'll continue to drive the science that makes cures possible.

DR. SUJUAN BA, PH. D.

A VISION FOR THE FUTURE

As the fight against cancer continues to evolve, so does the National Foundation for Cancer Research — adapting to emerging scientific trends and transformative technologies and incorporating state-of-the-art methodologies into its grant programs. NFCR has also diversified its fundraising efforts, through innovative campaigns and strategic partnerships with various organizations. This expanded financial support has further amplified NFCR's ability to fund groundbreaking research projects and attract top-tier scientists.

The foundation also has established educational programs and scholarships to nurture young talent and inspire the brightest minds to devote their careers to cancer research. Since 1973, NFCR has raised more than $410 million, making possible scientific breakthroughs that give patients hope for a cure. The first 50 years of the National Foundation for Cancer Research is a testament to the power of vision, determination and collaboration in the pursuit of a cure – and with the power of grassroots support of our donors.

From its humble origins starting with a $25 donation to being a major cancer-related charity, NFCR has impacted millions of lives. Driven by a steadfast commitment to innovation and global impact, NFCR continues to spearhead groundbreaking research that will shape the future of cancer care and ultimately lead to a cancer-free world. As NFCR moves forward, one thing remains certain: The unyielding spirit of its mission will inspire future generations.

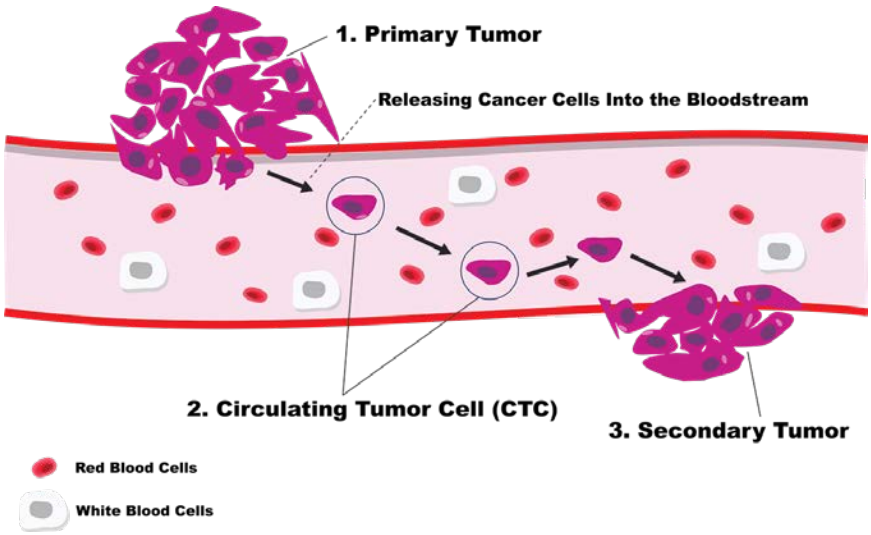
SCIENTIFIC PROGRESS

NEW RESEARCH PROGRAM IN CANCER CELL DIAGNOSTIC TECHNOLOGY

Advanced and metastatic cancer takes the lives of more than 90% of patients. Early detection of cancer and its progression is a dire unmet need for patients, families, and the cancer research community.

- Current approaches to cancer monitoring are invasive, time-consuming, and may not comprehensively represent the tumor microenvironment.
- In comparison, liquid biopsies are minimally invasive and, therefore, can be serially repeated to enable earlier detection of cancer progression Furthermore, liquid biopsies, specifically the isolation of live cancer cells, have overcome temporal and spatial heterogeneity associated with traditional biopsies.
- NFCR's new initiative focuses on cancer cell diagnostic technology to provide an increased understanding of the live cancer cells or circulating tumor cells (CTCs) in real-time and an inclusive understanding of the tumor microenvironment at the cellular, genomic, transcriptomic, and proteomic levels.

Ten leading researchers from across the globe have begun to generate the knowledge needed to accelerate this most critical cancer problem of early detection and monitoring of advanced cancer.



Circulating tumor cells (CTCs) detach from solid tumors and circulate in the bloodstream. Since they are live cells from a patient's tumor, they are considered a "liquid biopsy" of the tumor and offer the possibility assess in real-time, the tumor's characteristics, evolution, and response or resistance to treatments.

THANK YOU!

The National Foundation for Cancer Research wishes to thank the **Sorenson Legacy Foundation** for its generous support to expand on this critical research initiative. This joint partnership enables us to increase vital circulating tumor cell research that will benefit even more patients across cancer types.

SORENSON LEGACY FOUNDATION

COLORECTAL CANCER

Cultures of circulating tumor cells (CTCs) for functional tests and drug screening is one of the most promising applications, but it presents great technical challenges such as finding the right conditions to make the cancer cells grow outside of the host.

Dr. Cristofanilli is adjusting key factors like nutrients and oxygen levels and including endothelial cells of the microenvironment to better mimic the conditions in the blood-stream. The endothelial cells have enhanced the growth and increased the stability of the cancer cells. He will develop a pipeline for forming cultures of CTCs from patients with metastatic colorectal and breast cancer to enable high throughput drug screening (HTDS).

Massimo Cristofanilli, M.D.
Weill Cornell Medicine

IMPACT:

HTDS enables understanding the effect of multiple drugs on each patient's tumor and predicting which treatments or combinations would be more effective or resistant and identify new biomarkers to predict response.

KIDNEY CANCER

Renal cell carcinoma (RCC), the most lethal form of kidney cancer, afflicts >70,000 patients each year in the U.S. with a rising disease incidence. Molecular biomarkers which can help clinicians with treatment decision-making have been elusive, and currently no tissue-based testing is utilized for this disease.

Dr. Kotecha will study how treatment affects the yield and profiles of the circulating tumor cells. His team will conduct genomic profiling on the CTCs and on patients' tissues to compare gene mutations and test if dynamic changes in the amount and profile of CTCs associate with treatment response in patients.

Ritesh R. Kotecha, M.D. Memorial Sloan Kettering Cancer Center

IMPACT

These goals will provide the essential foundation to integrate this innovative CTC detection technology into the clinic to evaluate treatment effectiveness and fuel efforts to detect kidney cancer when this is not readily available on routine imaging.

PROSTATE AND KIDNEY CANCER

Neuroendocrine prostate cancer (NEPC) is an aggressive type of prostate cancer resistant to standard treatment and often underdiagnosed. **Dr. Beltran** will track gene expression patterns in CTCs of patients to develop an approach to detect NEPC and other subtypes.

Therapies for the most common type of kidney cancer, renal cell carcinoma (RCC), are not effective for patients with other subtypes who are often misdiagnosed.

Dr. Viswanathan will conduct genomic and RNA assays on the CTCs will characterize the molecular features of the subtypes of kidney cancer.

Srinivas Viswanathan, M.D., Ph.D. (top) and **Himisha Beltran**, M.D. Dana-Farber Cancer Institute

IMPACT

This team is developing the methods to detect the subtypes of these cancers in patients' CTCs. This will allow earlier detection of the subtypes and intervention with effective treatments.

MULTIPLE MYELOMA

Multiple myeloma (MM) is a blood cancer characterized by aberrant expansion of plasma cells in the bone marrow. Treatment can be very effective at controlling MM, relieving its symptoms and implications, and prolonging life. Unfortunately, MM is currently an incurable (terminal) cancer. Targeting MYC – a major cancer-causing protein in MM and many cancers - is challenging and known as "undruggable."

Dr. Kelliher will use a new compound that turns off the activation of MYC and slows growth in lab cell lines of the MYC-dependent MM.

Her team will test if the inhibitor stops the growth of circulating tumor cells isolated directly from MM patients.

Michelle Kelliher, Ph.D. University of Massachusetts, Worcester

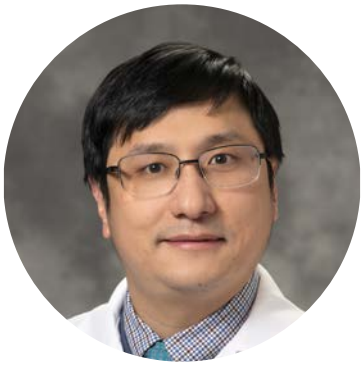
IMPACT

This research may bring a promising new approach to treat MM and other MYC- dependent cancers, including breast, colorectal, liver and prostate cancers.

PANCREATIC CANCER

Pancreatic cancer causes over 49,000 deaths each year in the US. Researchers do not have the tools to effectively detect the disease at an early stage. Moreover, the standard of care is only modestly effective and there are no biomarkers or tests to predict the patient's response.

With CTCs from pancreatic cancer patients, **Dr. Huang's team** will determine the expression of genes in the cells. They will use computational analyses to identify changes of gene expression patterns and correlate the expression with patients' responses to treatments.



Ling Huang, Ph.D.
Henry Ford Cancer Institute

IMPACT

Optimizing CTCs isolation procedures to readily apply in the clinics will help guide doctors to tailor therapeutic plans for individual patients, reduce adverse effects and ultimately, improve the outcome for patients.

WITH YOUR HELP, WE CAN MAKE CURES POSSIBLE FOR ALL CANCERS.

BREAST CANCER

Antibody Drug Conjugates (ADCs) are a new class of medications composed of 1) an antibody that targets a marker on cancer cells and 2) a linker to an active therapeutic agent for selective delivery of drugs preferentially to cancer cells.

Dr. Bardia led the clinical development of an ADC for triple-negative breast cancer. Other ADCs that target different markers are in development for other breast cancers. His team is utilizing patients' CTCs and tissue biopsy to develop a diagnostic test to detect the antigens (markers) on the cells in real-time. They have developed and optimized a protocol to stain the CTCs for various 'actionable' markers to use for matched therapy with ADCs for patients.

Aditya Bardia, M.D.
Massachusetts General Hospital;
Harvard Medical School

IMPACT

The diagnostic test can accelerate the development of novel precision ADCs for patients with metastatic breast cancer to guide selection of the "right drug" for the "right patient" and significantly improve their outcome.

SMALL CELL LUNG CANCER

Small cell lung cancer (SCLC) accounts for about one in seven cases of lung cancer and it afflicts over 33,000 patients per year and is rapidly fatal in 95% of cases. In most cases, chemotherapy is the only option to prolong survival, but when the cancer relapses it is resistant to most drugs. It is not known how the cancer becomes resistant, or how to overcome this, because there have only been very few living samples of the disease after relapse to study in the laboratory.

Dr. Drapkin's laboratory is using the detection technology to extract CTCs from blood samples of patients with SCLC to form models in the laboratory. His team has successfully formed one patient-derived model with other models beginning to grow. The treatment responses of these human tumors grown in the lab models mirror the responses of the patients themselves and can be used to compare different treatments.

IMPACT

By comparing SCLC cancer cells before and after patient's experience relapse, his team can understand how SCLC becomes resistant to our current drugs and develop new drugs to fight the disease.

Dr. Bersani is collecting SCLC CTCs to study the metastatic molecular features and establish a unique biobank of SCLC CTC cultures to investigate specific pathways responsible for metastasis. 3D culture conditions are being set up with CTCs and vascular cells to mimic how cancer cells interact with blood vessels and identify key mediators to target and interfere with metastasis.

Ben Drapkin, M.D., Ph.D.
University of Texas Southwestern

IMPACT

Understanding what drives the preferential destination of metastatic cells to certain organs may help clinicians to choose more tailored therapies and follow-up protocols, and scientists to develop better therapeutic strategies to reduce the recurrence of SCLC and improve the overall survival.

Francesca Bersani, Ph.D.
University of Torino, Italy

Although there are several treatment options for SCLC, there are no reliable tests, or "biomarkers," that identify tumors that will respond to specific treatments.

Dr. Rolfo's team has developed laboratory models from SCLC patients' CTCs, that replicate the behavior of the human tumor. This facilitates identifying specific molecular changes contributing to drug resistance. Standardizing this novel strategy of evaluating patients CTCs in the models will transform it into a reality.

Christian Rulfo, M.D., Ph.D.
Icahn School of Medicine
at Mount Sinai

IMPACT

This new approach may individualize treatment selection and develop a new approach for prolonging survival of patients with SCLC.

BECOME PART OF THE CURE WITH NFCR. WITH YOUR SUPPORT, WE CAN DEFEAT CANCER.

SCIENTIFIC PROGRESS

INNOVATIVE NEW THERAPIES

Collaboration is a bedrock principle of NFCR. It is how we can accelerate research advancements to realize an end to this terrible disease - through better prevention, diagnosis, and treatment. A future without cancer is possible.

NFCR has distinguished itself in the cancer research sector by emphasizing long-term, transformative research often overlooked by other major funding sources. NFCR promotes and facilitates collaboration among scientists to accelerate the pace of discovery from bench to bedside. One of the ways that NFCR promotes its mission is to provide unrestricted research support funds for outstanding cancer researchers.

In 2022, NFCR expanded its tradition and philosophy of facilitating collaborative research. Twelve teams of two experts, each team focused on a critical unmet need of patients, began collaborating and working together. The NFCR Team Science serves as a catalyst for expert scientists to work together – exchange ideas to launch and accelerate the most innovative and impactful research

WITH YOUR HELP, WE CAN MAKE CURES POSSIBLE FOR ALL CANCERS.

In order to maximize the impact of its support, NFCR supports novel high-risk research programs that might have the ability to dramatically change our understanding of cancer that, in turn, could lead to novel drugs, diagnostics, and therapies that will benefit cancer patients around the world.

- CAR-T Cell Therapy for Pancreatic Cancer
- Predicting Metastasis
- New Targets and Treatments for Triple-Negative Breast Cancer
- Targeted Therapies and Treating Lung Cancer Resistance
- Artificial Intelligence-based research
- Digital Spatial Profiler to better assess lung cancer biopsy tissue
- Gene Therapy and Cell Replacement
- Improving Immunotherapy for More Patients and Additional Cancer Types

PROGRESS IN TRIPLE-NEGATIVE BREAST CANCER

Dr. Coussens developed a combination of four therapies to enable immunotherapy to be effective for Triple-Negative Breast Cancer (TNBC) -the most difficult-to-treat breast cancer. In TNBC lab models, the four therapies increased immune response and caused the tumors to shrink.

New single-cell measurement technologies were applied to the tumor samples to characterize the response of specific cell types in the tumor microenvironment. **Dr. Fertig**, an expert computational biologist, created new artificial intelligence methods to analyze large datasets of genes and cells and identify the mechanisms causing the tumors to regress.

Results indicate that the therapies alter the microenvironment of breast cancer so immune cells can both reach and attack the tumor cells.

Lisa Coussens, Ph.D.
Oregon Health
& Science University

Elana Fertig, Ph.D.
Johns Hopkins University

IMPACT

The artificial intelligence approach to combine datasets from mouse models with those from human clinical trials enables identifying patients in which these same mechanisms occur, guiding doctors to identify patients who would respond to new immune-based therapies.

COMBATTING BRAIN METASTASIS IN BREAST CANCER

Kornelia Polyak, M.D., Ph.D.
Dana-Farber Cancer Institute

Patients with HER2-positive breast tumors (abnormal amounts of HER2 growth protein) are treated with targeted therapies but a subset of patients do not respond to treatment and develop progressive disease, including brain metastases associated with dismal outcomes.

Drs. Polyak and Weaver, pioneers in the tumor micro-environment, are exploring how the brain environment enables breast cancer cells to grow and survive.

Their data shows the sugar or glycosylation molecules in primary and metastatic cancers are distinct and are due to the microenvironment mechanical stress response.

- Cells in the brain interact with cancer cells and confer their resistance to HER2-targeting therapies.
- Cell interaction altered gene expression and changed the sugar coating of the cancer cells in the experimental models with similar changes also detected in patients samples.

Valerie Weaver, Ph.D.
University of California,
San Francisco

IMPACT

This new research field suggests that targeting glycosylation and brain cells-cancer cells interactions could improve patient outcomes.

ORAL CANCER & IMMUNE RESISTANCE

Teresa Davoli, Ph.D.
New York University
School of Medicine

Dr. Davoli previously showed that loss of a specific "p" region of chromosome 9p is more frequent in patients that do not respond to immunotherapy and can be utilized to stratify patients and decide clinical treatment. She and **Dr. Gutkind** want to understand the molecular mechanism underlying this effect.

The Davoli team engineered with the gene-editing tool, CRSIPR, several human cancer cell lines to contain or not the loss of genomic regions on chromosome 9p. They conducted computational analysis to decipher which 9p

genes are critical for immune evasion. Furthermore, Dr. Gutkind's team has begun experiments in mouse models to start dissecting the reason why tumors with 9p are less responsive to immunotherapy.

IMPACT

These studies will allow a better understanding of how tumor cells evade the recognition and attack by the immune system. Since 9p loss is a common feature of human solid tumors (especially common in oral, lung, melanoma and bladder cancers), these findings have the potential to help doctors identify patients who will respond or not to immunotherapy as well as improve current immunotherapeutic strategies.

J. Silvio Gutkind, Ph.D.
University of California, San Diego

HOW METASTASIS OCCURS & CANCER SPREADS

Metastasis (spread of cancer) is responsible for over 90% of cancer deaths and loss of quality of life.

Some people are more predisposed to metastasis than others. Among the metastasis-controlling genes discovered by **Dr. Welch**, the genes in the cell part called the mitochondrion, have sequences that differ by race. These different sequences identify a genetic explanation for why some people (ancestries) develop metastatic cancers more than other people/races.

Short RNA products or tRNA-derived fragments (tRF) have been identified from one mitochondrial gene in the mouse. This research aims to understand how tRF works and develop critical tools - a MINTmap - to compare data from the mouse with humans. **Dr. Rigoutsos** is developing the mouse version of a MINTmap to identify tRF in mouse tissues.

Dan Welch, Ph.D.
University of Kansas Cancer Center

IMPACT

This collaborative research will help explain racial disparities in cancer outcomes and help develop new anti-metastatic therapies and markers to determine a person's risk for metastasis.

Isidore Rigoutsos, Ph.D.
Thomas Jefferson University

IMMUNOTHERAPY FOR RARE SKIN CANCER, MERKLE CELL

While 50% of patients with Merkel cell carcinoma (MCC) respond well to immune-based therapies with long-lasting benefits, others do not. As with most cancers, the basis for different outcomes is unknown.

Approximately 80% of MCCs are caused by the Merkel cell polyomavirus, while 20% are caused by sunlight-induced DNA mutations. Each MCC subtype may be 'seen' in different ways by the immune system.

Drs. Topalian and Ngheim are using cutting-edge approaches to study gene expression in TILs (tumor-infiltrating cells), mechanisms of T-cell immunity will be identified in both types of cancer.

The research is identifying TILs in MCC biopsies from patients receiving immunotherapy. Computer modeling also revealed a gene expression profile derived from lung cancer mutation-specific T cells can also identify tumor-specific T cells in MCC specimens.

Suzanne Topalian, M.D.
Johns Hopkins University

Paul Nghiem, M.D., Ph.D.
University of Washington

IMPACT

A deeper understanding of the extent and type of immune cells in tumors responding or not to immunotherapy is now possible. This research will allow combinations of existing and emerging therapies to help patients overcome MCC and other virus-driven cancers.

NFCR RESEARCH IS 100% DONOR FUNDED. WITHOUT YOUR GENEROUS SUPPORT, CURES WON'T BE POSSIBLE.

PAIRING LUNG CANCER PATIENTS WITH THE RIGHT TREATMENT

Lung cancer patients with mutations in the ALK gene (ALK+) eventually become resistant to the 1st, 2nd, and 3rd line of standard therapies with no other available life-sustaining therapy. Further advances in new therapies are limited by how much data can be assessed using patient's tumor samples.

Drs. Hata and **Lin** are using a breakthrough technology that deeply identifies and quantifies the genes in cancer cells and tumor microenvironment in a standard tissue samples, a method not previously possible. The data suggests novel mechanisms driving ALK inhibitor resistance.

IMPACT

New targets in the tumor microenvironment can be used to develop entirely novel therapies to treat resistant cancers and give patients hope their lives will be saved.

Aaron N. Hata, M.D., Ph.D. (top)
Jessica J. Lin, M.D. Massachusetts General Hospital

NEW TARGETS FOR NOVEL TREATMENTS FOR TRIPLE-NEGATIVE BREAST CANCER

Androgen hormones contribute to growth and reproduction in men, and in women, too, although with smaller amounts. Some women with the difficult-to-treat Triple Negative Breast Cancer (TNBC) express high levels of the androgen receptor (AR.) Inhibitors of AR are standard therapy for prostate cancer but had little effect in TNBC patients.

To develop a treatment for these TNBC patients, **Dr. Haber's team** obtains sequencing and DNA (genomic) data and RNA (transcriptome) data from patients' CTCs. **Dr. Rheinbay's** lab analyzes the 'omic' data to identify genes, transcription factors, and DNA regulators that contribute to the lack of response of anti-androgens.

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Daniel A. Haber, M.D., Ph.D. (top)
Esther Rheinbay, Ph.D.
Massachusetts General Hospital

From blood samples, TNBC cells were isolated and then grown in culture.

- Unexpectedly, they discovered that AR-stimulating drugs completely halted cell growth of TNBC cells in culture.
- Research is underway to understand this surprising result.

IMPACT

This discovery has revealed a unique role for manipulating androgen signaling in TNBC and could lead to an effective treatment option, giving patients with AR-positive TNBC the hope they need.

WITH YOUR HELP, WE CAN MAKE CURES POSSIBLE FOR ALL CANCERS.

IMMUNE ACTIVATING THERAPIES FOR BREAST CANCER

Most women in the earlier stages of breast cancer choose a surgery that minimizes the amount of normal breast tissue removed. However, to prevent the cancer from returning, it is important that all the cancer is removed, and none is left behind. To address this unmet clinical need, this team has developed a dual-purposed targeted molecule that allows tumor visualization and treatment during surgery.

The team developed a lab breast cancer model and demonstrated a selective biomarker expressed on the model's primary and metastatic breast cancer. With a chemical probe that recognizes the biomarker, the scientists demonstrated activation of the probe after bound to the breast cancer slows the progression of cancer and decreases metastasis.

IMPACT

Probe activation will also turn on an immune response to attack the cancer. Future studies will test the potential benefit of combining the activation of this unique chemical probe with immune-activating therapies to provide a more durable response and permanent tumor immunity.

James Basilion, Ph.D.
Case Western Reserve University

John Letterio, M.D.
Case Western Reserve University

CAR-T CELL IMMUNOTHERPY FOR PANCREATIC CANCER

One of the most difficult-to-treat tumors is pancreatic cancer, as current treatments do not work well. There are currently no effective CAR-T cell therapies (or immune T cell-based therapies) for pancreatic cancer. **Dr. Posey** has designed CAR-T cell therapies that:

- Target CEACAM6, a tumor-associated antigen that contributes to immune suppression.
- Target CEACAM5 antigen, which also contributes to immune suppression.

Dr. Houchen is testing the therapies in patient-derived models.

Avery D. Posey, Jr. Ph.D.
University of Pennsylvania

Courtney W. Houchen, M.D.
University of Oklahoma Health Sciences Center

IMPACT

Targeting both CEACAM antigens may enhance the anti-tumor efficacy of these CAR T cells, increasing their ability to reach pancreatic cancer cells and preventing tumor escape. Evaluation of CAR-T cell performance in patient-derived tumor-bearing models reflects the potential to identify promising candidates for future clinical studies.

NOVEL APPROACHES TO SUPPRESS THE SPREAD OF CANCER

Seryl-tRNA synthetase (SerRS) is an essential protein that adds serine to help build proteins. It can also regulate different cell processes, such as preventing cancer growth and metastasis in lab models.

Drs. Schimmel and **Yang**, renowned experts in the tRNA synthetases, hypothesize SerRS boosts the activity of the immune system against cancer, and SerRS may directly stop cancer in its tracks by blocking key processes for cancer to survive and spread.

SerRS interacts with cancer cells directly:

- SerRS reduces Wnt signaling – a pathway which helps cancer cells migrate from the primary tumor and metastasize

Paul Schimmel, Ph.D.
Scripps Research

- SerRS interacts with cadherins – surface proteins that bridge cells to each other and their environment. Cancer cells naturally disrupt cadherins to migrate cells away.

IMPACT

SerRS research on boosting the immune system and direct interaction with cancer cells may lead to novel therapeutic applications to suppress the growth and metastasis of breast, brain, esophageal, kidney, rectal, stomach, and thyroid cancers.

Xiang-Lei Yang, Ph.D.
Scripps Research

IMMUNOTHERAPY FOR FATAL BRAIN CANCER, GLIOBLASTOMA

Chimeric antigen receptor (CAR)-T cell immune therapy has shown remarkable efficacy in blood cancers, but only limited benefits in GBM patients due to the limited infiltration into the brain and the immunosuppression in the GBM microenvironment. **Dr. Jain** previously discovered the drug, Losartan - widely used to control hypertension, reduces stress on blood vessels. In lab models of GBM, he showed lorsartan allows treatments to reach brain tumors, and made the tumor environment favorable for an immune system attack.

With **Dr. Suva's team**, experts in single-cell RNA analysis of GBM, they identified genes down-regulated by lorsartan that control these unfavorable properties.

Significantly, experiments combining agents similar to lorsartan with CAR-T cell immunotherapy slowed tumor growth and improved survival in GBM lab models.

Rakesh K. Jain, Ph.D.
Massachusetts General Hospital;
Harvard Medical School

Mario Suva, Ph.D.
Massachusetts General Hospital;
Harvard Medical School

IMPACT

Combining Losartan with CAR-T therapy could be an effective treatment for GBM. Since losartan is already FDA-approved, these findings could quickly lead to new clinical trials and potentially help patients with GBM.

GENE AND CELL THERAPY TO RESTORE VISION IN CANCER PATIENTS

Cancer patients endure treatments to fight their cancer and then some patients may suffer vision loss. Cancer-associated retinopathy (CAR) is a rare complication of cancer in which the body's immune response inadvertently also attacks the eye, resulting in permanent blindness. CAR can be diagnosed in different types of cancer: lung, breast, gynecologic, colon, pancreatic, skin, and prostate cancer.

Since the human retina cannot regrow itself after injury, this immune attack on the retina results in the permanent death of the rod and cone photoreceptors, the vision cells.

These two ophthalmologists, **Drs. Uyhazi** and **Aleman**, worked closely with scientists who developed the first gene therapy for a genetic disease (type of childhood blindness). They aim to transplant healthy and rod cone cells in the retina, in addition to gene therapy, to restore vision for CAR patients.

Their research has:

- Identified several new populations of developing photoreceptor cells in lab models
- Begun transplanting the healthy photoreceptor cells into model of retinal disease that mimics CAR in patients to better understand the ideal cell type to restore vision.

Katherine Uyhazi, M.D., Ph.D.
University of Pennsylvania

Tomas Aleman, M.D.
University of Pennsylvania

IMPACT

This pioneering research may lead to the development of new treatments to restore precious vision in cancer patients with retinopathy.

NFCR RESEARCH IS 100% DONOR FUNDED.
WITHOUT YOUR GENEROUS SUPPORT, CURES WON'T BE POSSIBLE.

AN EVENT THAT COULD CHANGE THE WORLD.

Dr. Monica M. Bertagnolli, NCI Director, Recipient of the 2023 AIM-HI Beacon Award for Women Leaders in Oncology.

Live Broadcast dialog between care advocates, cancer survivors, and researchers.

Dr. Isaac P. Witz, Recipient of the 2023 Szent-Györgyi Prize for Progress in Cancer Research, with Dr. Rakesh Jain and Dr. Sujuan Ba, Co-Chairs of the 2023 Selection Committee.

Daring to Explore an Understanding of Cancer as a Disease the Can be Cured!

On October 21, 2023 the Global Summit for Cancer Research and Entrepreneurship united some of the globe's most preeminent figures in cancer research, oncology care, and entrepreneurship to commemorate five decades of remarkable achievements, all while keeping a vigilant eye on the future and the shared goal of curing cancer.

Professor Isaac Witz of Tel Aviv University, was recognized as the recipient of the prestigious 2023 Albert Szent-Györgyi Prize. His pioneering work, as early as in the 1960s, paved the way for a deeper comprehension of the immune response within the tumor microenvironment, ultimately impacting tumor biology and growth. Professor Witz's contributions have led to paradigm-shifting revelations in the world of cancer research. His trailblazing work in tumor microenvironment research challenged established beliefs and reshaped our understanding of the intricate relationship between cancer cells and their surroundings.

The 2023 Global Summit for Cancer Research and Entrepreneurship brought together leaders from the entire oncology ecosystem - from academia, clinical care, industry, finance, science, and public policy, patients and the NFCR donor community, each sharing valuable insights and innovations in the fight against cancer.

LEARN MORE ABOUT THE GLOBAL SUMMIT FOR CANCER RESEARCH AND ENTREPRENEURSHIP AT NFCR.ORG.

MEET **NFCR LEADERSHIP**

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Department of Molecular Medicine Scripps Research

Dr. Sujuan Ba, CEO, and Brian Wachtel, Executive Director and Chief of Staff


Meeting of NFCR scientists with NFCR leadership and donors in Boston, 2023.

OUR CULTURE:

At NFCR our ultimate goal is to support pioneering cancer research in our quest to **make cures possible**. We do this by believing in **WE before ME**. Our team is comprised of thoughtfully considered individuals who all play an important role in helping to advance the mission.

GUIDING PRINCIPLES:

Act with Honesty and Integrity – NFCR is a trusted steward for our supporters' charitable giving. We responsibly distribute donor funds in order to maximize our impact toward our mission.

Value Teamwork and Collaboration – Whether it be with stakeholders, donors, cancer patients, or internal teams, we speak with open and respectful communications and extend professional courtesy to all partners. We believe we can accomplish more together.

Dare to Explore and Innovate – We are agile and entrepreneurial – we don't settle for the status quo; We strive for excellence in all aspects; we value new ideas and taking strategically considered risks that can improve and expand our reach.

Welcome and Value All Equally – We aim to be 'One NFCR' where we bring together diverse backgrounds and individuals to form a cohesive, powerful unit that believes in our shared vision for defeating cancer as we know it.

NFCR Staff ready to make cures possible!

NFCR SUPPORTS RESEARCH PROJECTS AT MAJOR ACADEMIC INSTITUTIONS AND MEDICAL CENTERS IN THE US, SUCH AS BELOW:

- Baylor University
- Case Western Reserve University
- Columbia University
- Harvard/DFCI
- Harvard/MGH
- Johns Hopkins University
- MD Anderson Cancer Center
- MIT
- New York University School of Medicine
- Oregon Health & Sciences University
- Scripps Research
- Memorial Sloan Kettering
- Mount Sinai Health System
- Thomas Jefferson University
- University of Kansas Cancer Center
- University of Oklahoma Health Science Center
- University of Pennsylvania
- University of Washington
- University of California, San Diego
- University of California, San Francisco
- University of Texas South Western
- University of Tornio
- Virginia Commonwealth University School of Medicine
- Yale University

WAYS TO **GET INVOLVED**

AND HELP MAKE CURES POSSIBLE.

WAYS TO GIVE and SUPPORT NFCR Champion for a Cure
Join our monthly giving program. This saves on fundraising costs, freeing up funds to sustain our scientists and makes it easy for you to consistently support lifesaving cancer research.

Honor & Memorial Giving
Give in honor of a cancer survivor or in memory of a loved one, your gift provides a meaningful tribute to someone whose life has been impacted by cancer.

Create a Legacy
Remember NFCR in your will or living trust. It's easy to arrange and may be changed at any time you choose through a provision or amendment prepared by your attorney.

You may also want to consider a Charitable Gift Annuity, which guarantees an income for life for a donor and/or a donor's spouse, with a portion eligible for tax deduction.

Create Your Estate Plan Online through NFCR with FreeWill
To make planned giving via your will or trust simple, we've partnered with FreeWill, a free, online estate planning tool that guides you through the process of creating your plans and legacy in less than 20 minutes.

Name your Own Cancer Research Fund
NFCR has been setting up designated and restricted fund programs for more than 40 years. These funds allow you to fund a specific researcher, project, cancer type or cancer research area in a significant fashion over a three year+ timeframe that will accelerate the pace of discovery.

Stock Gifts
Donating with long-term securities, including stocks and bonds, can offer significant tax benefits.

Charitable IRA Rollovers
Donate directly from your traditional or ROTH IRA. Donors must be at least 70 ½ years of age. Check with your attorney on the benefits of your IRA contribution.

Corporate Matching Gifts
Does your employer have a matching gift program? It is a great way to maximize oreven double your impact! Check with your HR Department for guidelines and gift matching forms. You can also discover more by visiting: **nfcr.org/employermatch**

Visit **www.nfcr.org/ways-to-give** to learn more about all of these (and more) ways to support NFCR in our fight against cancer.

NFCR is a 501(c)(3) tax-exempt nonprofit organization. Tax ID #: 04-2531031

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2024 PIONEER IN MEDICINE AWARD RECIPIENT

withum
ADVISORY TAX AUDIT

INDEPENDENT AUDITOR'S REPORT

To the Board of Directors of
National Foundation for Cancer Research, Inc. and Affiliates:

Opinion

We have audited the consolidated financial statements of the National Foundation for Cancer Research Inc. and Affiliates (collectively, the "Foundation"), which comprise the consolidated statements of financial position as of December 31, 2023 and 2022, and the related consolidated statements of activities, functional expenses, and cash flows for the years then ended, and the related notes to the consolidated financial statements.

In our opinion, the accompanying consolidated financial statements present fairly, in all material respects, the consolidated financial position of the National Foundation for Cancer Research Inc. and Affiliates as of December 31, 2023 and 2022, and the changes in their net assets and their cash flows for the years then ended in accordance with accounting principles generally accepted in the United States of America.

Basis for Opinion

We conducted our audits in accordance with auditing standards generally accepted in the United States of America ("GAAS"). Our responsibilities under those standards are further described in the Auditor's Responsibilities for the Audit of the Consolidated Financial Statements section of our report. We are required to be independent of the National Foundation for Cancer Research Inc. and Affiliates, and to meet our other ethical responsibilities, in accordance with the relevant ethical requirements relating to our audits. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Responsibilities of Management for the Consolidated Financial Statements

The Foundation's management is responsible for the preparation and fair presentation of the consolidated financial statements in accordance with accounting principles generally accepted in the United States of America, and for the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, management is required to evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the Foundation's ability to continue as a going concern for one year after the date that the consolidated financial statements are available to be issued.

Auditor's Responsibilities for the Audit of the Consolidated Financial Statements

Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance but is not absolute assurance and therefore is not a guarantee that an audit conducted in accordance with GAAS will always detect a material misstatement when it exists. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omission, misrepresentation, or the override of internal control. Misstatements are considered material if there is a substantial likelihood that, individually or in the aggregate, they would influence the judgment made by a reasonable user based on the consolidated financial statements.

In performing an audit in accordance with GAAS, we:

- Exercise professional judgment and maintain professional skepticism throughout the audit.
- Identify and assess the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, and design and perform audit procedures responsive to those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Foundation's internal control. Accordingly, no such opinion is expressed.
- Evaluate the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluate the overall presentation of the consolidated financial statements.
- Conclude whether, in our judgement, there are conditions or events, considered in the aggregate, that raise substantial doubt about the Foundation's ability to continue as a going concern for a reasonable period of time.

We are required to communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit, significant audit findings, and certain internal control-related matters that we identified during the audit.

Supplementary Information

Our audits were performed for the purpose of forming an opinion on the consolidated financial statements as a whole. The accompanying consolidating statement of financial position and consolidating statement of activities as of and for the years ended December 31, 2023 and 2022 are presented for purposes of additional analysis and are not a required part of the consolidated financial statements. Such information is the responsibility of management and was derived from and relates directly to the underlying accounting and other records used to prepare the consolidated financial statements. The information has been subjected to the auditing procedures applied in the audit of the consolidated financial statements and certain additional procedures, including comparing and reconciling such information directly to the underlying accounting and other records used to prepare the consolidated financial statements or to the consolidated financial statements themselves, and other additional procedures in accordance with auditing standards generally accepted in the United States of America. In our opinion, the information is fairly stated in all material respects in relation to the consolidated financial statements as a whole.

Withum Smith + Brown, PC

June 4, 2024

National Foundation for Cancer Research, Inc. and Affiliates
Consolidated Statements of Financial Position
December 31, 2023 and 2022

	2023	2022
Assets		
Cash	$ 1,756,768	$ 1,980,566
Accounts receivable	51,727	58,323
Prepaid expenses and other assets	373,196	483,324
Fixed assets, net of accumulated depreciation and amortization	20,192	29,069
Investments, at fair value	4,826,903	4,695,233
Amounts held in trusts by others, at fair value	2,658,016	2,427,684
Convertible note receivable	200,000	200,000
Right-of-use asset	649,897	847,904
Total assets	$ 10,536,699	$ 10,722,103
Liabilities and Net Assets		
Liabilities		
Accounts payable	$ 438,670	$ 631,769
Research contracts and grants payable	1,393,836	1,285,132
Accrued compensation and benefits	283,500	244,801
Lease liability	736,957	949,794
Total liabilities	2,852,963	3,111,496
Net assets		
Without donor restrictions	4,302,131	4,280,756
With donor restrictions	3,381,605	3,329,851
Total net assets	7,683,736	7,610,607
Total liabilities and net assets	$ 10,536,699	$ 10,722,103

The Notes to Consolidated Financial Statements are an integral part of these statements.

National Foundation for Cancer Research, Inc. and Affiliates
Consolidated Statements of Activities
Years Ended December 31, 2023 and 2022

	2023			2022		
	Without Donor Restrictions	With Donor Restrictions	Total	Without Donor Restrictions	With Donor Restrictions	Total
Revenue and support						
Public support	$ 7,183,362	$ 15,565	$ 7,198,927	$ 6,509,311	$ 111,693	$ 6,621,004
Bequests	1,469,533	-	1,469,533	1,124,995	-	1,124,995
Mailing list rental	102,377	-	102,377	86,700	-	86,700
Net investment return	773,689	-	773,689	(825,333)	-	(825,333)
Change in value of split-interest agreements	19,617	230,332	249,949	2,068	(605,816)	(603,748)
Other revenue	21,009	-	21,009	230,906	-	230,906
Net assets released from restrictions	194,143	(194,143)	-	191,468	(191,468)	-
Total revenue and support	9,763,730	51,754	9,815,484	7,320,115	(685,591)	6,634,524
Expenses						
Program services						
Cancer research	4,781,528	-	4,781,528	3,841,341	-	3,841,341
Public education and information	2,400,563	-	2,400,563	2,297,991	-	2,297,991
	7,182,091	-	7,182,091	6,139,332	-	6,139,332
Supporting services						
Fundraising	1,766,660	-	1,766,660	1,588,578	-	1,588,578
Management and general	793,604	-	793,604	729,147	-	729,147
	2,560,264	-	2,560,264	2,317,725	-	2,317,725
Total expenses	9,742,355	-	9,742,355	8,457,057	-	8,457,057
Change in net assets	21,375	51,754	73,129	(1,136,942)	(685,591)	(1,822,533)
Net assets						
Beginning of year	4,280,756	3,329,851	7,610,607	5,417,698	4,015,442	9,433,140
End of year	$ 4,302,131	$ 3,381,605	$ 7,683,736	$ 4,280,756	$ 3,329,851	$ 7,610,607

The Notes to Consolidated Financial Statements are an integral part of these statements.

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