

Spring 2023



## AN ANSWER IN *your genes*

Jenna, Roswell Park breast cancer patient

**F**or many cancer patients, understanding their genetics can make all the difference in their care. Research has shown that some cancers are hereditary. That means people who carry specific genes are at a higher risk of being diagnosed with certain cancers.

Patients who meet a set of criteria including history of cancer at a young age; rare cancer diagnoses; and a strong family history of cancers such as prostate, colorectal, breast, ovarian or pancreatic cancers are eligible for genetic testing at Roswell Park.

### Jenna's Story

Jenna Wier's mom was diagnosed with breast cancer at age 46. Thankfully, she completed her treatment, beat her disease and has been healthy ever since. Genetic testing helped to uncover why she had cancer at such a young age: she had the BRCA gene and was genetically predisposed to have breast cancer.

In 2017, Jenna's own genetic testing revealed that she too had inherited the gene. She diligently scheduled screenings until October 2021 when cancer came into her own life: stage 1b, triple negative breast cancer. While an aggressive form of cancer, hers had been found early and hadn't spread. She turned to the same Roswell Park doctor who had helped to save her mom. After 16 rounds of chemotherapy over approximately six months, Jenna completed treatment in April 2022.

"I'm so grateful to have known [about my genetic predisposition]," she said. "Who knows what would have happened? Knowing saved my life."

If her mom hadn't gotten sick, if she hadn't discovered her own genetic makeup, Jenna would have been completely blindsided by her cancer.

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Roswell Park donors fuel groundbreaking research, exclusive clinical trials, innovative technology and compassionate patient care programs.



# Herd of Hope

## TEAM SCIENCE AWARD 2022

(from left to right)

### THE TEAM:

Mark Long, PhD | Gurkamal Chatta, MD | Dominic Smiraglia, PhD | David Goodrich, PhD | Dean Tang, PhD



At Roswell Park, the Herd of Hope has been fueling team research initiatives driving cancer-fighting innovations since 2018. Each year, a grant is awarded to a team of investigators who are advancing scientific research that has the potential to save lives and change the way we treat cancer.

This funding would not be possible without the dedicated individual and corporate partners who are part of the Herd of Hope. These partners are spread out across Western New York, marked by the Herd's signature blue buffalos. These forward-thinking donors play a critical role in the fight against cancer at Roswell Park.

## Novel Strategies to Tackle Prostate Cancer Therapy Resistance and Extend Patient Survival

Led by Dean Tang, PhD

*George Decker Endowed Chair in Developmental Therapeutics  
Chair of the Department of Pharmacology & Therapeutics*

Current therapies to treat metastatic prostate cancer are, unfortunately, often short-lived. Even the most effective treatments often only work for two years before a patient's cancer recurs. One strategy that prostate cancer uses to escape the clinical therapies is called lineage plasticity — when cancer cells change to become resistant to treatment.

"Prostate cancer is the most prevalent cancer in men in the United States, with more than 250,000 annual new diagnosis," Dr. Tang said. "Each year more than 33,000 prostate cancer patients die from the disease."

"The high prostate cancer-specific mortality is not because cancer cells do not respond to androgen deprivation therapy (ADT) but rather because they rapidly develop resistance. Research from this team has uncovered a new mechanism to explain how prostate cancer cells become resistant to ADT. It will be very exciting and impactful to translate our knowledge of this new mechanism to treat patients."

### Improving Outcomes for Patients

Investigators at Roswell Park Comprehensive Cancer Center believe it's crucial to stop or even reverse cancer recurrence through therapies in order to improve outcomes for these prostate cancer patients and ultimately reach cures.

Dr. Tang and his team — David Goodrich, PhD, Gurkamal Chatta, MD, Dominic Smiraglia, PhD, and Mark Long, PhD — are seeking more effective, longer lasting treatments. With the support of the Herd of Hope, these researchers will dive into three interconnected projects, each aimed at uncovering the novel vulnerabilities surrounding the lineage plasticity of prostate cancer cells and how to stop it.



## Donor Support Drives Innovation

"The Roswell Park Alliance Foundation, through donor funding, has generously supported and played essential roles in many of our research projects," Dr. Tang said. "In 2017, we won a peer-reviewed Alliance Foundation Scientific Advisory Committee (SAC) grant, which allowed us to generate crucial laboratory data." That data led to two multiyear National Cancer Institute grants in 2018 and 2019 which empowered them to continue their work. Initial donor support made it possible for the team to acquire crucial pre-clinical data for the clinical trial led by Dr. Chatta, Professor of Oncology and Clinical Chief of Genitourinary Medicine, Dr. Tang said.

Together, this team seeks to find hope for prostate cancer patients in Buffalo and all around the world. The secrets of cancer they unlock could lead to practice-changing and survival-extending treatments that will shape the way we treat metastatic prostate cancer.



## Herd of Hope sparks multi-center collaboration

The team at Roswell Park is additionally collaborating with Samuel Denmeade, MD, at Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University and Hmisha Beltran, MD, at Dana-Farber Cancer Institute and Harvard Medical School.



Carl Morrison, MD, DVM  
Pathology Department

# R2T: Response to Therapy

An innovative blood test that will change the way we treat cancer

The way cancer is treated continues to change as innovative, new treatment options are discovered. Right now, most cancer patients receive three or four different treatments before finding one their cancer responds to. This can be chemotherapy, radiation, surgery, immunotherapy, experimental clinical trials or a combination of options.

With both chemotherapy and immunotherapy, it can be months or even a year before a patient finds out if their treatment path is working. If it's not working, a new treatment can be started but during this time, their cancer can grow and spread. With some cancers, patients might not have the luxury of time to wait these months to find out.

With cancer survivors, a person who has been free of disease for five years, there is no structured follow-up process once they've been labeled "cancer free." This means that cancer can reoccur, and patients might not know until they are very sick.

**What if there was an easier, less invasive and more accessible way to measure if a patient's treatment is working or if cancer has reoccurred in a cancer survivor?**

## Researchers at Roswell Park Comprehensive Cancer Center believe they have the answer

A routine blood test — combined with a novel technology developed at Roswell Park — could be all it takes to give doctors and patients real-time updates on treatment. It can become part of a survivor's annual routine check-up with their primary care physician to test for cancer recurrence.

Carl Morrison, MD, DVM, is leading the development of this innovative method he's calling Response to Therapy or simply, R2T. As Senior Vice President of Scientific Development and Integrative Medicine, Dr. Morrison is committed to bringing the most advanced and effective care to Roswell Park patients. He believes **R2T is the dynamic, convenient and cost-effective solution we've been waiting for.**

Dr. Morrison has already proven success in driving innovative, personalized medicine laboratory tests. With donor support, he led the creation of OmniSeq: comprehensive molecular and immune profiling mechanisms to help identify therapies that may be most effective for individual patients based on their genomic makeup. Roswell Park is one of only a few cancer centers to be able to routinely offer this testing.

## How will a blood test help?

Cells secrete DNA into your blood. The DNA of healthy cells looks different than the DNA of cancerous cells. Current available tests only have 15-20% accuracy in measuring the mutated DNA in a person's blood to indicate whether the amount of cancer in their body is changing.

Roswell Park's R2T uses the same principle of measuring cell-free DNA in the blood, but with proprietary technology that offers **three to five times more accuracy than other methods, delivering data with 95% accuracy.** Because the amount of healthy cell DNA outnumbers the amount of cancer cell DNA in the blood, this novel technology is critical to provide reliable results.

If a patient's blood is tested after each treatment, their doctor can determine in real time if the cancer is increasing, decreasing or staying the same. There would be no need to wait months for an MRI or CT scan to see how the treatment is progressing; they could monitor the disease visit by visit, week to week.

**"There's still a lot of work to do here," Dr. Morrison says, "but I really believe the technology we have will become a nationally accepted procedure."**



## Two studies underway at Roswell Park

A phase 1 study is funded in part by donations already underway at Roswell Park. Dr. Morrison and his team are engaging in an observational, non-interventional study for patients with early-stage cancers. The researchers are using R2T to monitor cell-free DNA before and after patients undergo surgery to remove their tumors.

They started with stage 1 and stage 2 cancers to solidly demonstrate the superior sensitivity which sets R2T apart from other industry tests. **"Since our test is designed to be significantly more sensitive than others, we should be able to prove it in very early-stage cancers," Dr. Morrison explains.**

Dr. Morrison also has plans for two concurrent studies once donations are secured. First is a study for current patients with advanced disease. These patients will be monitored every three weeks during therapeutic treatment to watch for increasing, decreasing or plateaued levels of cell-free DNA. The second is a study for cancer survivors to test for disease recurrence.

Overall, this is a fast-paced and aggressive path toward higher quality cancer care, knowing we cannot waste time as cancer certainly does not.

**"R2T has the opportunity to change the treatment of cancer as much as anything I've ever witnessed in my life."**

**-Dr. Morrison**

## Your support is helping advance the pace and expand the reach of R2T

Completely changing the landscape of cancer care does not come without cost. With donor support, this Response to Therapy technology has the potential to save lives, improve quality of life and ease the financial burden of cancer treatment on patients. This is unlike any advancement we have ever seen. You are an important part of a new path in the fight against cancer.

# Donor funding paves the way for innovative research

Many of the world-class scientists at Roswell Park have new research ideas that could change the course of cancer treatment and lead to cancer cures. But without appropriate funding, their ideas would never get off the ground and become lifesaving standards of care. Roswell Park's Scientific Advisory Committee (SAC) seeks to bridge this gap.

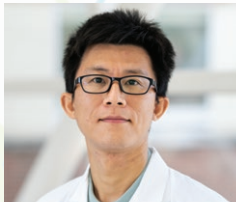
Donations to the SAC initiative provide seed funding for new projects and can be made to fund research for a specific type of cancer. Researchers submit their applications to compete for donated funds and an internal, objective committee decides which projects receive funding. The projects funded in fall of 2022 included:

## PROSTATE CANCER

### TARGETING PROSTATE CANCER VULNERABILITIES WHEN IT METASTASIZES TO THE BONE

Led by Hai Wang, PhD

In 60-90% of men, advanced prostate cancer cells metastasize to the bones, significantly decreasing quality of life and increasing the risk of mortality. Dr. Wang wants to uncover the vulnerabilities of prostate tumors in the bone, beginning by studying how cancer cells utilize lactate in an unconventional way, to hopefully address both issues for these patients who experience a great deal of pain and risk mortality.



Hai Wang, PhD

### LEVERAGING METABOLIC STRESS IN PROSTATE CANCER TO IMPACT THE EPIGENOME

Led by Dominic Smiraglia, PhD

Patients with advanced stage prostate cancer often relapse as their tumor adapts to treatment and becomes resistant. Dr. Smiraglia will leverage metabolic stress to target that method of adaptation tumor cells take. His investigation will improve our understanding of how that adaptation is made possible and provide a foundation for new ways to stop it.



Dominic Smiraglia, PhD

### FINDING WAYS TO ELIMINATE CHANGES IN PROSTATE CANCER THAT DEVELOP RESISTANCE

Led by Dominic Smiraglia, PhD

Androgen deprivation therapy is commonly used to treat prostate cancer but most patients relapse when their cancer cells become resistant to treatment. Dr. Smiraglia plans to study just how those cells change their identities by epigenetic means to abandon their dependence on androgen to grow. Understanding this process will clear a path forward to eliminating that resistance in prostate cancer, improving success for patients.

## BREAST CANCER

### A PROMISING NEW SOLUTION TO HER2 THERAPY RESISTANT BREAST CANCER

Led by Boyko Atanassov, PhD

The overexpression of a particular protein is a major factor in HER2 therapy resistant breast cancer. Indirectly targeting that protein by inhibiting its regulators could be a promising solution to limiting resistance to treatment. Dr. Atanassov seeks to uncover the role of these regulators in HER2 therapy resistant breast cancer in order to ultimately introduce more effective treatment options for patients.



Boyko Atanassov, PhD

### REVEALING THE SECRETS OF CHEMO-RESISTANT TRIPLE NEGATIVE BREAST CANCER

Led by Jia Fang, PhD

Triple negative breast cancer is the most aggressive kind of breast cancer. One treatment option is chemotherapy, but resistance often develops. Dr. Fang will look at an epigenetic regulator during triple negative breast cancer's response to chemotherapy to reveal novel DNA repair mechanisms and also potentially identify this regulator as a potential biomarker to predict chemotherapy response of this cancer in the future.



Jia Fang, PhD

## LUNG CANCER

### ROLE OF INNATE LYMPHOID CELLS IN SEXUAL DISPARITY OF LUNG CANCER INCIDENCES

Led by Prasenjit Dey, PhD

Public health efforts dedicated toward tobacco cessation have led to a decline in rates of lung cancer among males. There has been a slower decline among females and new instances among female non-smokers are on the rise. Dr. Dey is investigating why this is happening to find ways to target lung cancer more effectively for female patients, who are at higher risk.



Prasenjit Dey, PhD

### ESTABLISHING THE EFFECTS OF OBESITY ON THE FUNCTION AND METABOLIC ACTIVITY OF REGULATORY T CELLS

Led by Joseph Barbi, PhD

Non-small cell lung cancer causes 20% of all cancer deaths in the US and has a 5-year survival rate of only 24%. Besides smoking, obesity is recognized as an amplifying factor for both disease risk and negative outcomes in many cancers. Dr. Barbi aims to uncover how obesity drives tumor progression by fueling regulatory T cells and tumor-aiding immune suppression in patients with non-small cell lung cancer.

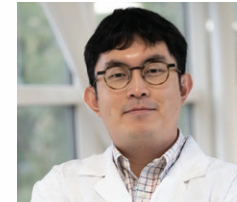


Joseph Barbi, PhD

### FINDING NEW WAYS TO OVERCOME RESISTANCE USING GENE OVEREXPRESSION SCREENING

Led by Dae-Kyum Kim, PhD

One tumor-driving gene called KRAS is found in many cancers and, more specifically, one-third of all lung cancers. There is an existing treatment to inhibit one widespread variant of KRAS after first-line therapy like chemotherapy, but the results in patients vary. There is not an existing therapy that can inhibit KRAS and all its variants at once. Dr. Kim seeks to better understand how these variants become resistant in order to stop them proactively. He and his team expect their approach will lead to the discovery of novel therapies and prognostic biomarkers for cancer patients with rare gene overexpression.



Dae-Kyum Kim, PhD

## BLOOD CANCERS

### STUDYING THE COMBINATION OF TWO THERAPIES TO REACH MORE PATIENTS WITH ACUTE MYELOID LEUKEMIA

Led by Pamela Sung, MD, PhD

Existing treatment options for patients with acute myeloid leukemia (AML) are not effective individually for all patients. Dr. Sung has conducted initial research to point to the potential success of a combination of two existing therapies, which could reach the patients who would otherwise have developed resistance to one of those treatments alone.



Pamela Sung, MD, PhD

### USING PROTEIN INHIBITOR COMBINATIONS TO IMPROVE TARGETED THERAPY IN ACUTE MYELOID LEUKEMIA

Led by Pamela Sung, MD, PhD

A protein called FLT3 is frequently mutated in AML and causes an aggressive form of the blood cancer. Treatments are available to target this particular protein, but they don't work for some patients. Dr. Sung aims to find out more about this protein's interaction with AML on a molecular level. This will help to improve options for that subset of patients in need of an effective treatment and could also improve existing treatment options.

## OTHER CANCERS

### SEARCHING FOR NEW TREATMENTS FOR PANCREATIC CANCER

Led by Michael Feigin, PhD

Pancreatic ductal adenocarcinoma is a deadly cancer with a 5-year survival rate of 11%. Dr. Feigin and his colleagues have discovered a potentially new, non-toxic therapy option for these patients who need effective treatment options. Researchers hope to develop more effective inhibitors and learn if their new approach can potentially stand alongside existing standard of care therapies.



Michael Feigin, PhD

### STUDYING THE EFFECTS OF ULTRAVIOLET LIGHT AND IMMUNOSUPPRESSION ON CUTANEOUS SQUAMOUS CELL CARCINOMA

Led by Gyorgy Paragh, MD, PhD

Ultraviolet (UV) light exposure is a critical risk factor for cutaneous squamous cell carcinoma (CSCC), the second most common cancer in the United States. Dr. Paragh's team is establishing the relationship between early UV-damaged cell groups in the skin and CSCC risk in immunosuppression to help identify individuals most at risk for CSCC. They are also focused on establishing the efficacy of early topical treatment before immunosuppression to reduce the risk of CSCC.



Gyorgy Paragh, MD, PhD



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## Carly's Story

The first several months of Carly Hathaway's illness were frustratingly without answers. While out on a hike in August of 2020, she began to feel discomfort which turned to pain. Thinking she may have pulled a muscle in her glutes, she remained active throughout the summer without finding any way to effectively address her symptoms.

Carly was an otherwise healthy young woman. Her primary care doctor didn't seem alarmed, but Carly knew something wasn't right. She advocated for herself, trusted her instincts and ultimately learned she had stage 3 colorectal cancer. After beginning her care elsewhere, she moved her care to Roswell Park in October where she took full advantage of the Young Adult Program, mental health support and genetic testing.

There's a significant history of cancer in Carly's family, but her results did not show any genetic link. She was concerned that there seemed to be no clear reason why she would have cancer at such a young age, but Carly was glad to have a path forward through her treatment. Now, she's determined to use her own experience to help educate and advocate for other young people with concerns about their health.

## Offering answers

Funds raised by individuals, the Future of Roswell Society and through events like the 2022 IceCycle help fund Roswell Park's genetics program. Genetic testing was able to offer answers for both Jenna and Carly, which helped their care teams form the best possible plan for their cancer journeys. Genetic testing can help clinicians better tailor treatment to each patient individually and knowing personal genetics can help inform next steps in care, in many cases.