

Spring 2018

## From Shock to a *Deeper Purpose:* LIVING with Ovarian Cancer



**W**hen Kathleen went under anesthesia in May 2004, it was for laparoscopic surgery for endometriosis.

But what she woke up from was sudden and radical surgery for stage 3c ovarian cancer.

When her gynecologist began the laparoscopy, “he discovered I was loaded with cancer, and those are his words,” Kathleen says. “He called Dr. Lele, who came to Buffalo General and operated on me. I believe Dr. Lele delayed his vacation to do this.” (Shashikant Lele, MD, FACOG, is Clinical Chief of Gynecologic Oncology at Roswell Park.)

Kathleen began treatment immediately, qualified for a clinical trial and went into remission for 10 years. Advanced ovarian cancer is difficult to eradicate, so she has been called a miracle. But she now has had two recurrences, in 2015 and 2017, and has undergone radiation as well as more chemo and surgery. Her latest scan showed no detectable cancer.

It’s been a journey of many ups and downs, and Kathleen credits her family and her faith for getting her through it.

She and her husband, Roy — her high school sweetheart — just celebrated their 44th anniversary. “That man sits with me through every treatment, and some of them take six hours. He never complains. He’s my biggest supporter and cheerleader, my right hand,” she says. They have two children and four granddaughters they adore. Kathleen has two sisters she’s very close to. And her dad just turned 90.

But Kathleen says she has found both help and joy in the many people of Roswell Park, too. First there’s Dr. Lele and his staff. “They’re just beautiful people. **It amazes me that Roswell is able to hire so many people who are so compassionate and who feel like family.**”

She got a pretty wig, a nice hat and a lot of support from the Wig and Head Covering Boutique in the Resource Center, all of which are made

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From left, Drs. Richard Koya, Kunle Odunsi and Thine Chodon with genetically engineered T cells to be given to a patient as part of a new adoptive cell therapy clinical trial at Roswell Park.

## EXPLORING A NEW IMMUNOTHERAPY APPROACH WITH DONOR SUPPORT

“Cancer cells are really smart,” observes Richard Koya, MD, PhD. “Chemotherapy, radiotherapy, surgery and even some immunotherapies may have some effect initially, but cancer cells have a way to evade them, to be resistant and grow back. That’s why it’s so difficult to treat cancer.”

As Associate Director of the Center for Immunotherapy and Director of the Vector Development and Production Facility at Roswell Park, Dr. Koya spends a lot of time thinking about new strategies to help the human immune system outsmart cancer. One of those strategies, developed by Dr. Koya and Kunle Odunsi, MD, PhD, FRCOG, FACOG, Deputy Director of Roswell Park Comprehensive Cancer Center and

Executive Director of the Center for Immunotherapy, aims to deliver a two-pronged attack against cancer cells by super-charging the patient’s immune system.

The therapy is being studied in patients for the first time anywhere in the world through a phase 1 clinical trial at Roswell Park, for which Dr. Koya serves as Scientific Principal Investigator and Dr. Odunsi as Clinical Principal Investigator.

“What we see over and over in trying to treat some of the most aggressive and intractable cancers, including many lung, brain, ovarian, breast, melanoma and sarcoma tumors, is that the tumor fights back,” says Dr. Odunsi. “The area around the tumor is a hostile

environment that disarms immune cells and deprives them of the ability to kill tumor cells. We have identified a major pathway by which these kinds of cells try to disable immune cells, and formulated a strategy for exploiting that weakness.”

This trial was made possible thanks to donations to Roswell Park as well as funding from the National Institutes of Health. Supporting groundbreaking research like this gives our scientists the opportunity to develop cutting-edge treatments that could make all the difference for our patients.

### “Super Immune Cells”

In a process similar to a blood donation, a patient’s T lymphocytes, or T cells — which are part of the immune system and help the body fight disease — are collected and sent over to Roswell Park’s Center for Immunotherapy. There the team alters (or “engineers”) the T cells and multiplies them to create “an army of super immune cells.” The cells are then given back to the patient through an infusion.

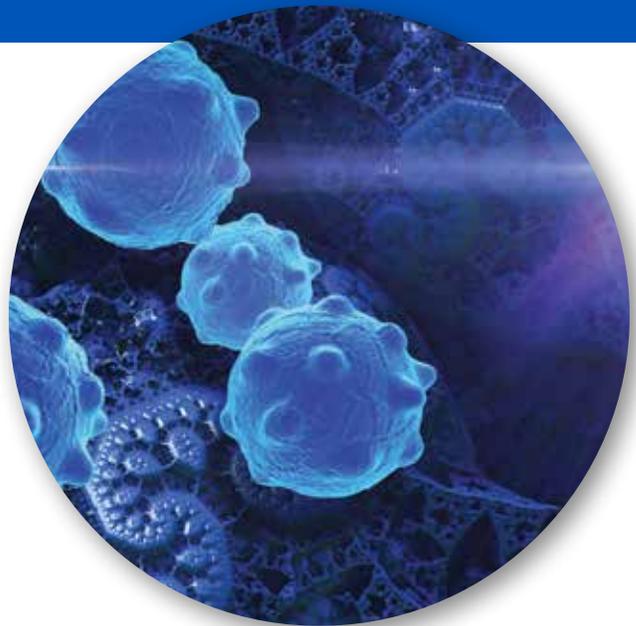
So how does the team engineer these cells to fight cancer? Think of it like they’re providing the cells with specialized weapons designed to target cancer cells as well as special armor to protect them during their fight.

- **Step 1:** They arm cells with specific T cell receptors that enable the T cells to hunt down and destroy tumor cells that express a specific substance that is only found in cancer cells.
- **Step 2:** The team adds a second gene to protect the T cells from attack from a protein that tumors use for protection.

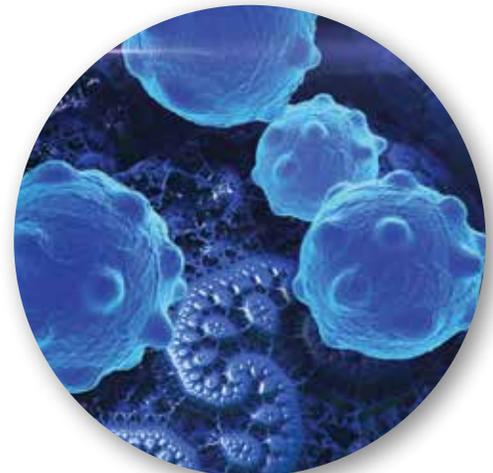
“Nobody else is doing the combination of these two different elements in the same platform anywhere in the United States or even on the planet,” says Dr. Koya.

Donations from friends like you allow Roswell Park to take advantage of emerging research opportunities like this and pursue promising clinical trials that may lead to new standards of care and save more lives.

“The promise of outsmarting cancer and disarming its defenses by ramping up our own innate immune systems — and in ways that can benefit large numbers of patients with various types of cancers — has never been more real,” adds Dr. Odunsi.



*A nurse administering immunotherapy treatment at Roswell Park.*



# Fourteen New Research Projects Launched

## Thanks to Donor Support

Your gifts are helping groundbreaking new research take flight at Roswell Park.

Twice a year, the Alliance Foundation's Scientific Advisory Committee (SAC) announces a call for grant applications to Roswell Park's research community. These grants provide seed funding for our researchers to launch ideas that have demonstrated the potential to impact patient care and save lives. This past fall the committee received 51 applications and, after conducting a competitive peer-review process, awarded 14 grants to the projects determined to have the most promise for finding cancer cures and saving lives.

Here are the 14 projects that were selected by the SAC to receive these grant awards, totaling \$1,342,938:

### 1 Triple Negative Breast Cancer

Triple negative breast cancer (TNBC) is very aggressive and has so far eluded treatment. More than 50 percent of TNBCs overproduce a molecule called epidermal growth factor receptor (EGFR). Our group has identified a recombinant human protein that inhibits EGFR in this subset of breast cancer and diminishes the growth of cancer cells. This study will evaluate the protein's therapeutic importance in TNBC, potentially leading to a new treatment for this difficult cancer.

— Boyko Atanassov, PhD, and Yuesheng Zhang, MD, PhD, Department of Pharmacology and Therapeutics

### 2 Immunotherapy in the Aging Immune System

Adrenergic stress — the type of stress that can activate the fight-or-flight response — has long been suspected of promoting cancer by suppressing the natural anti-tumor immune response and by stimulating tumor growth. The Repasky lab will study whether reducing these stress signals inhibits cancer growth by stimulating the immune system. Our results so far have helped to launch a new clinical trial design that may benefit patients in existing immunotherapy clinical trials.

— Elizabeth Repasky, PhD, Department of Immunology

### 3 Immunotherapy

Clinical studies of SurVaxM immunotherapy in glioblastoma led us to a breakthrough in regard to the fundamental biology of survivin, the cancer molecule targeted by this vaccine. We discovered that a portion of survivin is located on the surface of cancer cells and thus is targetable by several alternative modalities, most notably antibody and CAR T cell-based immunotherapies. These novel agents are highly effective at killing tumor cells, and their development into new clinical therapeutics holds great promise for treating many different forms of cancer.

— Michael Ciesielski, PhD, Department of Neurosurgery

### 4 Prostate Cancer

In our study, we will explore whether targeting a population of cancer stem cells with novel therapies combined with the standard-of-care therapies will delay, prevent or overcome resistance to treatment for certain prostate cancers. If successful, we will begin clinical trials at Roswell Park.

— Dean Tang, PhD, Department of Pharmacology and Therapeutics

### 5 Metastasis

Metastasis is the most common cause of death in patients with melanoma and certain other cancers. We will investigate the effectiveness of a particular biomarker in predicting and monitoring response to treatment with — and side effects from — immune checkpoint inhibitors in patients with advanced cancer. If successful, this will help improve treatment effectiveness and extend our patients' life spans.

— Fumito Ito, MD, PhD, Department of Surgical Oncology and Center for Immunotherapy

### 6 Melanoma

The common beta-blocker propranolol has been shown to aid in cancer treatment by blocking the action of adrenergic stress, which promotes tumor growth and inhibits tumor-specific immune responses. We will investigate whether we can improve patient immune and clinical response to immune checkpoint inhibitors by adding propranolol to treatment. Not only could this result in better treatment for our patients, but it could reduce their financial burden as well.

— Marc Ernstoff, MD, Department of Medicine



## 7 Breast Cancer

We recently discovered that a particular type of immune cell weakens the effect of immunotherapy in breast cancer by preventing expansion of the army of T lymphocytes needed to destroy tumor cells in metastatic lesions. In this project, we will explore the mechanisms by which this happens. Ultimately we hope this information will help us improve outcomes for our immunotherapy patients.

— Sharon Evans, PhD, Department of Immunology

## 8 Research in Our Community

Our project's goal is to develop culturally appropriate methods and guidelines for the collection, storage and use of bio-specimens for cancer research in collaboration with local Native American community partners.

— Elisa Rodriguez, PhD, MS, and Rodney Haring, PhD, MSW, Department of Cancer Prevention and Control

## 9 Cancer Prevention and Control

It is well-proven that physical activity provides real benefits for cancer patients, but too often they don't stick to their regimen. In our research we will apply a novel therapeutic brain stimulation approach currently being examined in smoking cessation research, with the hope of helping cancer patients comply better with their exercise regimens.

— Christine Ambrosone, PhD, Department of Cancer Prevention and Control

## 10 Immunotherapy

While immunotherapy has revolutionized cancer treatments, some types of cancer and some patients still do not respond well. Because tumors seem to be able to inhibit the activity of the immune cells called T cells, we will examine how RNA processing in T cells could affect immunotherapy. We hope our results will improve the effectiveness of these treatments.

— Scott Olejniczak, PhD, Department of Immunology

## 11 Exploring New Radiation Therapy Treatments

We will establish clinical trials testing the safety and efficacy of new tumor-shrinking therapies combined with novel stereotactic body radiation therapy (SBRT). Our projects will explore the effects of radiation on the immune system and examine mechanisms including how tumor inflammation may be caused by the ability of cells to recognize damage to DNA and how stress influences the efficacy of radiation.

— Anurag Singh, MD, Department of Radiation Medicine; Andrei Gudkov, PhD, DSci, Lyudmila Burdelya, PhD, and Sandra Gollnick, PhD, Department of Cell Stress Biology; Elizabeth Repasky, PhD, and Jason Muhitch, PhD, Department of Immunology; Pawel Kalinski, MD, PhD, Department of Medicine; and Marina Antoch, PhD, Department of Pharmacology and Therapeutics

## 12 Pediatric Cancer

Many types of pediatric tumors are caused by chromosomal abnormalities. However, the molecular mechanisms underlying formation of this type of tumor are still not well understood. We seek to explore how these abnormalities cause tumor generation and help accelerate research in this area.

— Asoke Mal, PhD, Department of Cell Stress Biology, and Eugene Yu, PhD, Department of Cancer Genetics and Genomics

## 13 Genetics and Genomics

Next-generation sequencing is a DNA technology that allows us to search for the genetic alterations in multiple genes that cause human cancers. In order to maintain our role as a major cancer center, it is necessary to build Roswell-specific tumor sequencing programs, or "pipelines." We will pilot the development of a Roswell-specific pipeline focusing on ovarian cancer — an area of particular scientific strength at Roswell Park.

— John Krolewski, MD, PhD, Department of Cancer Genetics and Genomics

## Experimental Therapeutics

### 14a Pancreatic Cancer

We are examining potential new drug targets with the hope that targeting them will be more successful than current methods in combating pancreatic ductal adenocarcinoma.

— Michael Feigin, PhD, Department of Pharmacology and Therapeutics

### 14b Oncolytic Viruses

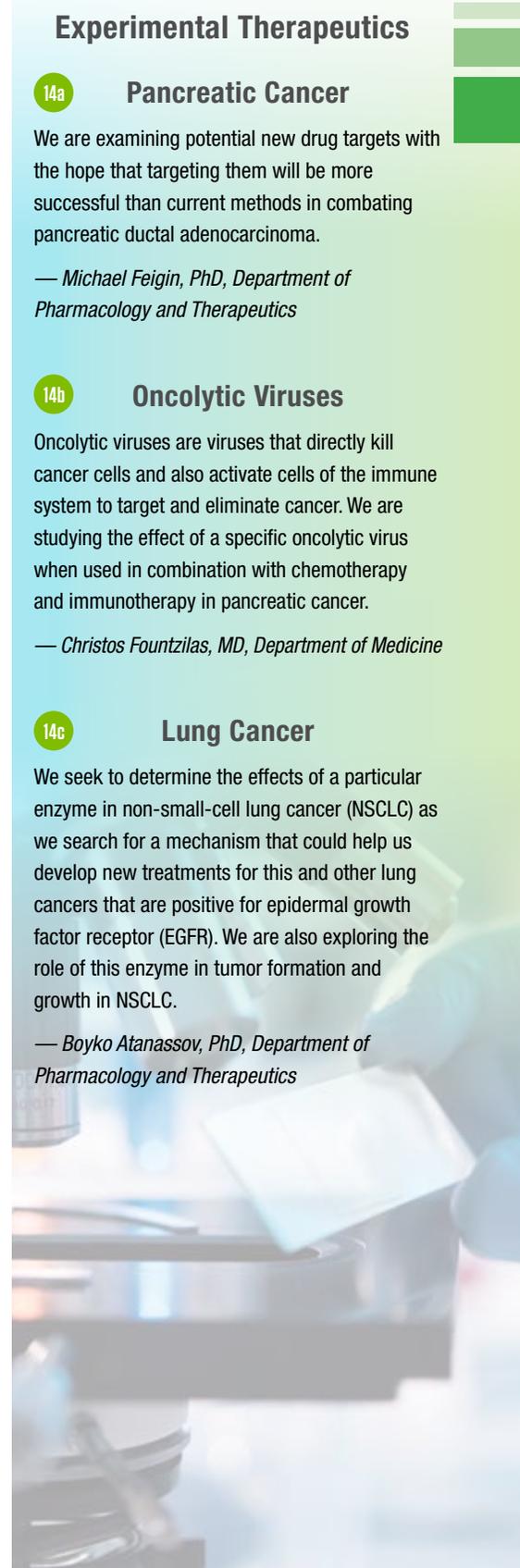
Oncolytic viruses are viruses that directly kill cancer cells and also activate cells of the immune system to target and eliminate cancer. We are studying the effect of a specific oncolytic virus when used in combination with chemotherapy and immunotherapy in pancreatic cancer.

— Christos Fountzilias, MD, Department of Medicine

### 14c Lung Cancer

We seek to determine the effects of a particular enzyme in non-small-cell lung cancer (NSCLC) as we search for a mechanism that could help us develop new treatments for this and other lung cancers that are positive for epidermal growth factor receptor (EGFR). We are also exploring the role of this enzyme in tumor formation and growth in NSCLC.

— Boyko Atanassov, PhD, Department of Pharmacology and Therapeutics



# Quality of Life Programs at Roswell Park

Roswell Park knows how important it is for patients to be able to put their focus on their cancer fight. We also know how critical it is to have positive distractions at the right times and remember that cancer does not define you. That's why, thanks to generous donor gifts, we fund more than 30 quality-of-life programs each year that help patients get through their battle while finding some joy and escape in the smaller things.

Artists-in-Residence is one of those programs. To entertain patients, relieve stress and help them stay active, Roswell Park's Artists-in-Residence make the rounds among the clinics and all the inpatient areas, including the BMT Center, offering art, music and even dance activities to those who are interested and feel well enough to participate.

**Here are two stories about about the impact a little creativity and connection can have in our patients' lives.**

## A Little Art Makes a Big Difference

Chelsea Crane comes into the patient room with color on her mind and beads in her carrying case. One of Roswell Park's five Artists-in-Residence, she's here to provide some creative escape for the patient staying here.

That patient, Lisa, is no stranger to creativity. She shows Chelsea some rocks she has painted — rocks she picked up walking on the beach at Sturgeon Point on Lake Erie, New York.

They're big rocks, about 6-8 inches across. Lisa has decorated them with nature scenes — a waterfall with a bridge and a heart-carved tree on one; a stream with trees and a rabbit on the other. She has made them as gifts for her doctors. "You want them to know that you care for them as much as they care about you," she says.

As a lymphoma patient at Roswell Park, Lisa is spending several weeks in her hospital room preparing for a bone marrow transplant, instead of at home painting or walking the beach. So when she sees Chelsea come in with her stacks of art supplies, she lights up.

Lisa digs happily through bins of colored beads, picks stones in earth tones and begins to string them together into window decorations. She and Chelsea talk while they make colorful art together.

Why does Lisa like these visits? "It takes your concentration off having tubes in you," she says.

Chelsea, a dancer with a master's degree in social work, finds herself humbled by her interactions at Roswell Park. "As an Artist-in-Residence, I'm able to connect with others in such a unique way," she says. "We're able to build our interactions upon art, and I find that this allows people to communicate through a language we don't often access."

"I always find it touching when a patient says that for a moment they forgot they were in a hospital because I know that the creative interactions are making a difference. Our team of Artists-in-Residence are truly thankful to all the donors and supporters of our program because it allows us to continue fostering healing interactions."

— Chelsea Crane, Artist-in-Residence





Hand-painted postcards designed by patients as part of the donor-funded Artists-in-Residence program.

## You've Got Mail

For the past three years, Barb Murak was an unofficial messenger for Roswell Park patients recovering from a blood or marrow transplant (BMT). Pulling a handcart filled with art supplies, from time to time the Artist-in-Residence stopped by an inpatient room to deliver a surprise. “Knock, knock!” she called out. “You’ve got mail!”

Barb would reach into a folder and select a colorful, hand-painted postcard with a cheerful message written on the back.

The person who created the card might be another patient, the loved one of a patient, or a caregiver. But after the card reached its destination, Barb would invite the recipient to create a new card and send it on to someone else, building another link in a chain of good wishes.

The project was inspired by a woman named Pat, who grew bored and restless while recovering from a BMT in 2014. Not having a variety of things to do is a common challenge for BMT patients,

because they remain in the hospital for several weeks after the transplant. They are at high risk for infection during this period, so they can’t leave their rooms except while getting exercise by walking laps around the hallway. And unlike inpatients in most other areas of the hospital, they can’t visit with one another to pass the time.

One day when Barb stopped in at her room, Pat confided, “I wish I could talk to the other patients on the floor. Can I write a note to someone to say, ‘I’m thinking of you’?” The two quickly came up with an idea: to build connections between BMT patients by inviting them to decorate a blank postcard — and maybe add a few words of encouragement.

Some of the paintings the patients make are simple; some are intricate. Some cards are blank on the back, and others are inscribed with inspirational words. But every one sends the same message: **Someone cares about you. Pass it on.**



**QUALITY OF LIFE PROGRAM**  
FUNDED BY DONATIONS

Roswell Park's Quality of Life Fund is supported by the Ralph C. Wilson Jr. Foundation and the generosity of our donors.

### *The Artists-in-Residence Program*

Five artists participate in the program and include specialists in visual arts, dance and music. The program is part of the Arts in Healthcare Initiative conducted in partnership with the University at Buffalo. Barb Murak has just retired from the program, so we thank her for her years of service to our patients and their quality of life!





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possible by donations to Roswell Park. “Not only did they provide me with a hat and a wig,” she says, “but they also provided me with courage and a smile. I left with a smile on my face and a positive attitude.”

And then there are the other patients Kathleen has connected with. And through them, she has discovered a purpose in her cancer.

**“With pain, either you become bitter or better. I chose to become better.** It’s only when you can focus in on the blessings and how good God has been to you throughout the years that you can put a smile on your face and realize that there’s a purpose in what you’re doing,” Kathleen says. “I have challenged myself to encourage other people. I pray for people to come to me and that I can help. I feel like my cancer has a purpose.”

She also knows the critical role the generous contributions of Roswell Park donors have played in her battle.



Thank you, dear donors, for giving to the Wig and Head Covering program so that I can fight this disease with dignity. Thank you for selflessly giving so clinical trials, research, new treatments and quality-of-life programs can continue to be available to people who you will never meet or know.

“If it wasn’t for kind and generous contributors who have been led to give financially to this wonderful organization, I most likely would not be here, continuing to fight.

