If it weren’t for SurVaxM, I never would have met three of my four grandchildren.”

In June 2016, John woke up in the middle of the night in convulsions from a seizure. After EMTs rushed the 66-year-old husband, father and grandfather to a Syracuse hospital, doctors discovered a tumor in his brain. He had glioblastoma, a brain cancer that has poor prognosis and few treatment options. Average life expectancy is 15 months after diagnosis.

Luckily for John, something critical was happening just a few hours west at Roswell Park, thanks to support from donors like you. The SurVaxM vaccine had begun its phase 2 clinical trial for newly diagnosed patients. After surgery to remove as much of the tumor as possible, he found out he qualified for the trial. His son and family lived in Buffalo, so each trip meant he got to spend time with them. And he desperately wanted more time.

That was three and a half years ago. Now, in early 2020, John just got back from a trip to Aruba with his wife. He exercises four times a week and will be visiting his grandchildren again soon.

John credits the donor-funded SurVaxM trial with every precious minute of this extra time.

A New Phase

Now many more glioblastoma patients around the world will have the same chance John did.

An agreement between MimiVax LLC and Chinese healthcare group Shanghai Fosun Pharmaceutical (Group) Co., Ltd., will enable further development of SurVaxM for patients in the U.S. and China. MimiVax is a Roswell Park spinoff founded in 2012 by Robert Fenstermaker, MD, Chair of the Department of Neurosurgery and Director of the Neuro-Oncology Program at Roswell Park, and Michael Ciesielski, PhD, Department of Neurosurgery, to develop SurVaxM and other immunotherapies. It is developing SurVaxM based on technology originally developed through donations and licensed from Roswell Park.

SurVaxM is a vaccine that kills cancer cells by targeting a protein called survivin, which is prevalent in the cells of glioblastoma and many other cancers as well. “SurVaxM puts cancer cells in a Catch-22,” says Dr. Fenstermaker. “After vaccination, the immune system kills tumor cells that express survivin. If the tumor cells turn survivin off to escape the vaccine, they stop growing and become more susceptible to chemotherapy.” The vaccine is given to clinical trial participants in conjunction with standard chemotherapy.

Donor giving has been critical in all phases of development

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Herd of Hope Pursues Next Big Cancer Breakthrough

Thanks to Community Support

Kevin Guest House while receiving daily radiation treatments at Roswell Park. On Friday, Jennifer would return to Buffalo to bring him home. This strenuous schedule went on for seven weeks while Andrew received 33 radiation treatments.

“I gave up tucking my kids in at night,” he says. “I missed walking them around on Halloween trick-or-treating. I am a very hands-on dad and have never spent time away from my family. After treatments continued and I became very weak, I missed telling them goodnight and that I loved them, as I often felt asleep early in the evening. I missed their first day of school and didn’t get to meet their teachers at meet-the-teacher night.”

I found myself often very depressed and missing my family. The feeling of loneliness was stifling and made getting up and heading to treatment dreadfully every day until Friday, when I knew that I would soon see my family. Dealing with coming to grips with your cancer and your new future was made even tougher by the overwhelming feeling of loneliness.

“After treatment, I would often go sit on the third floor, as I dreaded going back to the quiet of my room,” Andrew says. “The hustle and bustle of the hospital reminded me of my family.”

How might the stress of his cancer diagnosis and distance from his family, as well as the added stress to his wife, affect Andrew’s health and treatment outcomes? How can we help patients manage stress like his or counter its effects? That’s what Christine Ambrosone, PhD, Betty Repasky, PhD, Elizabeth Bouchard, PhD, and the rest of the team that received the 2019 Herd of Hope Team Science Award want to find out (see sidebar for full list of team members).

Herd of Hope brings the Western New York community together in pursuit of the next big cancer breakthrough. Individuals and companies can purchase a blue buffalo statue to display as a sign of their commitment to Roswell Park and to helping save lives through the kind of cutting-edge cancer research possible only at an NCI-designated comprehensive cancer center.

Roswell Park researchers competed for the $500,000 prize funding a project with the potential to impact the way we diagnose, prevent and treat cancer. Following a competitive review by a committee of scientific leaders, the project headed by Dr. Ambrosone was chosen for this community-driven grant.

“An Interdisciplinary Approach to Understanding How Stress Affects the Cancer-Immune Equilibrium and Patient Outcomes”

This study will comprise four projects investigating different aspects of the connection between stress and cancer. The researchers’ goal is a grant from the National Cancer Institute to establish a Center of Excellence in Stress and Cancer Research at Roswell Park. This goal would not be possible without this initial funding from donors. The projects include:

1. Investigating interactions between chronic stress, the way tumors develop, and the role of the immune system in survival outcomes.
2. Examining whether feeling cold is a marker of adrenergic stress and immunosuppression and testing the potential link between sleep disturbance and adrenergic stress-mediated immunosuppression. (Adrenergic stress is any kind of stress that can activate the fight-or-flight response.)
3. Exploring the roles of various stressors on cancer patients and their caregivers as well as how both adapt to stress.
4. Evaluating the impact of exercise as a stress-reduction strategy, and examining whether physical activity changes biomarkers of adrenergic stress, immunosuppression and nervous system control.

“Our team is grateful to members of the WNY community for contributing to this award, which will allow us to build the capacity to conduct research studying how stressors can affect cancer growth and progression,” says Dr. Ambrosone. “Bringing together scientists from different disciplines, including immunology, cell stress, sociology, epidemiology and physical therapy, our team science approach will hopefully broaden our understanding of how stress can affect patient outcomes and, importantly, how we may intervene to reduce stress responses in patients.

“We believe that this ‘it takes a herd’ approach will allow us to develop psychological, behavioral, immunological and pharmacological strategies to reduce adrenergic stress and assess how these strategies affect patient outcomes and survivorship.”

The leaders of the Herd of Hope team science project are:

Christine Ambrosone, PhD, Roswell Park Alliance Foundation Endowed Chair in Cancer Prevention; Chair, Department of Cancer Prevention and Control
Elizabeth Repasky, PhD, the William Huebsch Professorship in Immunology; Department of Immunology
Elizabeth Bouchard, PhD, Department of Cancer Prevention and Control
Scott Abrams, PhD, Department of Immunology
Marina Antoch, PhD, Department of Pharmacology and Therapeutics
Kristopher Attwood, PhD, Department of Biostatistics and Bioinformatics, Co-Director, Biostatistics and Statistical Genomics Shared Resource
Rikki Canioto, PhD, Department of Cancer Prevention and Control
Fanqiu Gu, PhD, Department of Cancer Prevention and Control
Chi-Chen Hong, PhD, Department of Cancer Prevention and Control
Megan Failier, PhD, Department of Psychosocial Oncology
Andrew Ray, PT, PhD, Department of Cancer Prevention and Control
Song Yao, PhD, Department of Cancer Prevention and Control

Visit RoswellPark.org/Giving or call 716-845-4444 to make a donation today.
How do we go about making the big changes the world needs in diagnosing, preventing and treating cancer? We start with big ideas — the kind that percolate in the minds of scientists right here at Roswell Park. Donations from generous supporters like you allow Roswell Park to award critical seed funding that helps these big, bright ideas develop into real data and treatments.

Twice a year, our Scientific Advisory Committee (SAC) calls on the Roswell Park research community for grant applications. The committee members — an objective group of Roswell Park scientists — then score the applications and select the projects they think have the most potential to make the greatest impact on the cancer landscape.

This past fall, the committee received 37 submissions. Eight grants were awarded to explore ideas and make research progress that could create big changes for cancer patients everywhere.

**PANCREATIC CANCER**

Pancreatic cancer is one of the most lethal cancers because there are few treatments that are effective against it. With the help of this grant award, a new study will explore how a poorly understood protein called HNF1A promotes this cancer’s resistance to drugs targeting the protein KRAS, which is believed to drive more than 90% of all pancreatic cancers. It will also determine whether drugs called BET-inhibitors could improve the effectiveness of current treatments and save more lives from this deadly disease.

“Understanding and Overcoming HNF1A-Driven Drug Resistance in Pancreatic Cancer,” led by Ethan Abel, PhD, Department of Molecular and Cellular Biology

**TRIPLE NEGATIVE BREAST CANCER**

Triple negative breast cancer (TNBC) is an aggressive type of cancer, with high incidence of metastatic progression. Understanding how tumors escape the primary cancer site to form distant metastasis will help begin to prevent this spread. Roswell Park researchers have discovered a fundamental connection between the metabolism of GTP — a building block of our nucleic acids — and the metastatic process. This grant will allow for close investigation aimed at understanding how a rate-limiting enzyme for GTP production supports invasion, with the ultimate goal of developing novel ways to prevent deadly metastasis.

“Novel Interactions at the Cell Membrane of the GTP Biosynthetic Enzyme Inositol Monophosphate Dehydrogenase 2 (IMPDH2) Control Tumor Invasiveness,” led by Alina Bianchi-Smiraglia, PhD, Department of Cell Stress Biology

Unfortunately, there are currently no targeted therapies for TNBC patients, and the majority of patients become resistant to the chemotherapy. Researchers have detected a cancer-specific energy-generating enzyme that is very active in aggressive TNBC. When this enzyme activity is elevated, TNBC patients experience the worst outcomes of recurrence and metastasis. If we find strategies to inhibit this powerful metabolic enzyme, we can potentially discover new ways to combat TNBC recurrence or metastasis.

“Targeting Metabolic Enzyme PFKFB4 in Triple Negative Breast Cancer,” led by Subhamoy Dasgupta, PhD, Department of Cell Stress Biology

One of the factors determining how tumors grow is a protein known as the cellular gatekeeper, p53 tumor suppressor. But it also is frequently mutated and either is inactivated or becomes a tumor promoter in cancer, including 65%-85% of TNBCs. Researchers seek to shed light on how another protein, known as PEPD, could be used to trigger mutated p53’s tumor-suppressing actions. This research could revolutionize understanding of the biology and regulation of p53 mutants, identify a novel therapeutic strategy in cancers and generate data important for obtaining national funding for further research to develop PEPD-based therapeutic strategies in cancer.

“Reactivating p53 Mutants for Cancer Treatment by Targeting PEPD,” led by Yuesheng Zhang, MD, PhD, Department of Pharmacology and Therapeutics

The Roswell Park Alliance Foundation has awarded over 500 grants to promising research studies thanks to donors like you.

We know that TNBC patients who have no remaining signs of cancer after their first treatment regimen (known as pCR, or pathologic complete response) have improved survival rates overall. But they only comprise 25%-35% of TNBC patients. Through a phase 1 clinical trial, we will test a new combination of medications that we believe will produce an increased rate of pCR, better prognoses and decreased need for more intensive chemotherapy. The results will enable us to pursue national grant funding that will allow us to conduct further clinical trials of this drug combination.

“Mobilizing the Immune System to Reduce the Need for Chemotherapy and Improve Outcomes in Triple Negative Breast Cancer,” led by Shipra Gandhi, MD, Department of Medicine

One of the factors determining how tumors grow is a protein known as the cellular gatekeeper, p53 tumor suppressor. But it also is frequently mutated and either is inactivated or becomes a tumor promoter in cancer, including 65%-85% of TNBCs. Researchers seek to shed light on how another protein, known as PEPD, could be used to trigger mutated p53’s tumor-suppressing actions. This research could revolutionize understanding of the biology and regulation of p53 mutants, identify a novel therapeutic strategy in cancers and generate data important for obtaining national funding for further research to develop PEPD-based therapeutic strategies in cancer.

“Reactivating p53 Mutants for Cancer Treatment by Targeting PEPD,” led by Yuesheng Zhang, MD, PhD, Department of Pharmacology and Therapeutics

**METASTATIC BREAST AND Pancreatic Cancers**

Metastatic breast and pancreatic cancers are among the leading causes of cancer death in the United States. This study will investigate the effectiveness of a two-drug combination that has never been tested before. It will selectively target breast and pancreatic cancers that have a genetic alteration in a tumor suppressor called p53. With the data generated, researchers can launch a phase 1 clinical trial to test this new regimen, with the goal of improving patient outcomes and saving more lives from these devastating diseases.

“Selective Synthetic Lethality Strategy for p53-Deficient Breast and Pancreatic Cancers,” led by Andrei Bakir, PhD, Department of Cancer Genetics and Genomics

**BREAST CANCER IN AFRICAN-AMERICAN WOMEN**

Black women who develop breast cancer have poorer prognoses than white women with the disease and are more likely to develop estrogen-receptor negative (ER-) breast cancer, which is harder to treat. This may be partly due to having multiple children and a lower rate of breastfeeding, which could result in abdominal cells accumulating in breast tissue. The hypothesis is that when these cells become cancerous, they will develop into ER- breast cancer. The results will reinforce education initiatives and hopefully lead to new preventative measures for women who don’t breastfeed.

“Impact of breastfeeding on breast cancer incidence and survival in African-American women,” led by Angela Omilian, PhD, Department of Cancer Prevention and Control

I am excited that this project was selected for funding by the Roswell Park Alliance Foundation and wish to thank the donors for their generous support. Previous funding by the Foundation made it possible for me to successfully compete for funding from the National Cancer Institute and has allowed me to pursue promising research leads.

—— Dr. Zhang
You know how terrible it is when you get the flu. Especially at this time of year. But it doesn’t last long. Your immune system leaps into action, and in a few days, you’re starting to get back to normal. Why doesn’t the immune system act that way against breast cancer? That’s part of a bigger question that got some Roswell Park researchers thinking, especially in relation to brain-metastatic breast cancer (BMBC), which has few treatment options and poor outcomes. Fortunately, those researchers and their teams are in the right place to investigate that question. Enter Dr. Shipra Gandhi.

Who Is Dr. Gandhi?

Shipra Gandhi has known since she was a child that she wanted to help people. The daughter of two physicians, she was fascinated to hear her parents discuss their cases. It soon became clear how meaningful it would be to help not just individual patients but humanity as a whole in the always-changing medical field.

Thanks to donor giving, she now holds a position that is critical for researchers thinking, especially in relation to brain-metastatic breast cancer: Breast Cancer Translational Researcher. The Roswell Park Alliance Foundation was presented with the need to fund this position and immediately saw its importance.

What Is a Translational Researcher?

A Translational Researcher serves as a bench-to-bedside bridge, using the results of laboratory research to develop clinical trials that will lead to techniques and tools that will help improve, extend and save lives of cancer patients. This particular Translational Researcher is overseeing a promising and important new study. Dr. Gandhi is principal investigator (PI) on a clinical trial that was funded by the Department of Defense (DoD) through a Breast Cancer Research Program grant awarded to Pawel Kalinski, MD, PhD, Vice Chair for Translational Research in the Department of Medicine and Rustum Family Professor for Molecular Therapeutics and Translational Research, and his colleagues at Roswell Park and Moffitt Cancer Center in Tampa. The four-year, $6.42 million, highly competitive Breakthrough Award will fund a phase 2 clinical trial in patients with brain-metastatic breast cancer. In her role as PI, Dr. Gandhi works closely with Dr. Kalinski.

This trial will be the first to study the effectiveness of a three-pronged therapeutic strategy developed by Dr. Kalinski in collaboration with Brian Czerniecki, MD, PhD, Chair of the Breast Oncology Department at Moffitt, and by their clinical research teams at both institutions. Moffitt is another highly ranked, National Cancer Institute-designated comprehensive cancer center and member of the National Comprehensive Cancer Network. A companion clinical trial will move forward at Moffitt with additional DoD funding. Both trials will be available to patients at both cancer centers.

Now back to that bigger question. How do we get the immune system to treat BMBC like it does the flu? For our scientists, this leads to another question: Why does checkpoint blockade immunotherapy work in cancers like melanoma but not in breast, and what can we do about it? Dr. Kalinski and his team, including Dr. Gandhi, developed a platform that convines the immune system “to become as aggressive and effective in treating breast cancer as it typically is in treating flu.”

“We developed a platform using mediators of antiviral responses to convince the immune system to really go after cancer and to treat it as if it were a flu infection,” says Dr. Kalinski.

Checkpotenf blockeec immunotheerapy helps to optimize the immune system’s attack on cancer using drugs called immune checkpoint inhibitors. Immune cells and some cancers have proteins that work to keep the immune system in check. These drugs block the proteins, releasing the brakes on the immune system and improving the cancer-fighting effect.

“I was highly motivated and impressed when I observed the Roswell physicians take such great care of patients, and, at the same time, also work on research to find new cures for those who are in the utmost need.”

— Dr. Gandhi

This fall Dr. Gandhi also received a SAC grant for her project proposal to determine how chemotherapy agents can increase the ability of immunotherapies to fight triple negative breast cancer. See page 5 for more.
What's Next?
Shanghai Fosun Pharmaceutical (Group) Co., Ltd., and MimiVax will pursue clinical development of SurVaxM for patients in the U.S. and select territories in China. Initial support from Fosun will enable and partially fund the upcoming pivotal clinical trials in both the U.S. and China.

Based upon positive results from initial phase 1 and phase 2 studies, the team expects to advance to a large, multicenter randomized phase 2 trial in the coming year. The previous phase 2 study of 63 patients with newly diagnosed glioblastoma has demonstrated significantly longer survival time for patients treated with SurVaxM, with 93.5% alive a year after diagnosis, compared with expected 65% survival based on historical studies. John was part of that phase 2 study.

Donor support has been critical in SurVaxM’s development and progress from the very beginning. “We’re so grateful for the community’s generous and enthusiastic support of this work,” says Dr. Fenstermaker. “The initial laboratory investigations that paved the way to where we are now would not have been possible without donor support.”

Hope for Other Cancers
Because of the success of the early phase studies, additional clinical trials of SurVaxM for multiple myeloma and neuroendocrine tumors are underway at Roswell Park. A pediatric and high grade glioma trial is also under development. Because survivin is present in other cancers as well, there may be more opportunities for treatment.

Patients like John have continued hope for more time thanks to generous giving to Roswell Park.

“Since I’ve been on SurVaxM, I’ve had three new grandchildren, and there’s another boy on the way,” John says. “I hope it will help extend others’ lives or cure them. So far it’s extended mine probably more than two years over what it would have been if I hadn’t come to Roswell.”

To learn more about the SurVaxM agreement, visit tiny.cc/RoswellSurVaxM.