# Impact Today



#### Issue 5, Fall 2020

### Letter from the President



As we enter December, it has become clear that the disruption to the world's cancer research enterprise caused by the COVID-19 pandemic is a troubling, durable trend.

At Gateway we also see an inspiring trend that is even more durable – the incredible innovation of cancer researchers

everywhere in finding ways to advance their lifesaving work during this pandemic and beyond. Rethinking the prevailing centralized clinical trial model, investigators are proposing decentralized trial designs that leverage today's technologies to bring cancer clinical trials to patients' doorsteps. Collectively, the research community is reimagining the way clinical trials are conducted to safeguard against disruption from the COVID-19 pandemic and future public health emergencies.

Just as cancer doesn't stop for a pandemic, neither does innovation in cancer research. My colleagues at Gateway and I are inspired and motivated to find new ways to support your research with upcoming grant opportunities such as our second Gateway Discovery Grant and our Decentralized Clinical Trials Initiative, which you'll read about in this issue. What are your ideas for advancing cancer treatments and cures? Please visit our website today to submit a grant application and share this newsletter with your colleagues so they're aware of Gateway funding and collaboration opportunities.

Finally, November was Pancreatic Cancer Awareness Month, reminding us that new treatments are desperately needed for one of the most lethal cancer types. In this issue of *ImpactTODAY* you'll read about a multi-center trial of a promising approach to easing the severe pain associated with pancreatic cancer and you'll hear from patients about how this trial is restoring their quality of life. Currently enrolling patients, the trial offers opportunities for multisite collaboration.

From the entire Gateway team, thank you for your dedication to innovation on behalf of the patients we serve and your partnership in moving us closer to ending cancer as we know it.

Sincerely,

Michael

Michael Burton President and CEO, Gateway for Cancer Research

# REPORT FROM THE RESEARCH AND GRANTS COMMITTEE

Gateway's Research and Grants Committee convenes quarterly to advance the most promising grant proposals to Gateway's Board of Directors for full funding decisions. At its most recent meeting, the committee reviewed and scored a total of 15 projects: nine new proposals and six decentralized clinical trial applications. All from NCI-designated comprehensive cancer centers, the new proposals were in targeted therapies, immunotherapy, pediatrics, and rare cancer types, including:

- Assessing the safety and tolerability of combining venetoclax and selinexor with chemotherapy in pediatric patients with relapsed or refractory acute myeloid leukemia
- Evaluating a medical device that delivers systemic amplitude modulated radiofrequency electromagnetic field therapy to improve outcomes for patients with progressive metastatic bladder cancer post cisplatin-based chemotherapy and PD1/L1 inhibitor therapy

- Determining the safety, feasibility, and possible efficacy of supplementing the damaged immune systems of patients with advanced, metastatic solid tumors with allogeneic white blood cell infusions from young, healthy donors
- Examining the overall safety and effectiveness of a low-cost intradermal therapeutic cancer vaccine to treat underserved women with metastatic breast cancer living in poorly resourced, developing countries
- Investigating whether pre-operative high dose proton radiotherapy in combination with pembromizulab elicits an immune response in node-positive, high-risk HR+ breast cancer patients
- Developing a "hybrid decentralization" early phase clinical trials model to improve the democratization of study participation and "future-proof" clinical trials from disruption caused by ongoing and future epidemics
- Exploring the safety and tolerability, and evaluating the anti-tumor activity of an MDM2/MDMX inhibitor in combination with paclitaxel in patients with advanced or metastatic solid tumors with wild-type TP53 and HR+ breast cancer
- Assessing whether stereotactic radiotherapy delays progression and improves outcomes in patients with oligometastatic adenoid cystic carcinoma
- Testing the safety and efficacy of a central nervous system-permeable PARP inhibitor in combination with temozolomide chemotherapy to treat patients with recurrent IDH1/2-mutant gliomas.

#### Gateway thanks all investigators who submitted grant proposals.

Do you have an innovative idea for a Phase I or Phase II clinical trial? Visit **GatewayCR.SMApply.org** and apply online today.



## FEATURE SPOTLIGHT



## Fueling the Engine of Cancer Discovery *Upcoming Grant Opportunities*

Since its inception nearly 30 years ago, Gateway has invested more than \$90 million in over 180 innovative cancer research clinical trials. Gateway focuses exclusively on patient-centered cancer research that improves treatment outcomes while maintaining quality of life.

Gateway is committed to supporting clinician-scientists in their work to end cancer as we know it. While funding proposals are continuously accepted on a rolling grant application basis, below are two unique upcoming grant opportunities.

#### **Decentralized Clinical Trials Initiative**

When Gateway launched its new Decentralized Clinical Trials Initiative this past spring the response from top cancer centers in the U.S. and abroad was overwhelmingly positive.

Due to this high interest, Gateway is focusing much of its funding on decentralized clinical trials.

Gateway will award grants in early phase, patient-centered, clinical oncology studies that leverage technologies like telemedicine, remote monitoring and wearables to bring clinical trials directly to patients at home.

To apply today, visit **GatewayCR.SMApply.org** and select "GFCR Decentralized Grant Program" to begin your application.

#### Gateway Discovery Grant Program

In 2019, Gateway for Cancer Research announced a scientific partnership with Conquer Cancer<sup>®</sup>, the ASCO Foundation, to establish the *Gateway Discovery Grant Program*. The biennial \$1.5 million award supports early phase clinical trials with the greatest potential to advance breakthrough cancer research. The first *Gateway Discovery Grant*, awarded in 2020, focused on immunotherapy.

The 2022 *Gateway Discovery Grant* will provide three to five years of funding to catalyze innovative clinical research with a strong potential impact on mitigating cancer health disparities. The Phase I or Phase II clinical trial may include the study of any cancer type and must propose research that will contribute to the improved diagnosis and/or treatment of cancers found to disproportionately affect underrepresented populations.

To help improve equitable care for all people with cancer, this second *Gateway Discovery Grant* will support research that specifically aims to reduce disparities related to factors such as race and ethnicity, age, gender, geography, education and other socioeconomic indicators that may impact outcomes.

The 2022 *Gateway Discovery Grant* will be awarded June 2022. The application period is now open, and Letters of Intent (LOIs) are being accepted through March 15, 2021. To apply, please visit **ASCO.org/Gateway**.

For questions about the Decentralized Clinical Trials Initiative, the *Gateway Discovery Grant*, or other funding opportunities please email **Research@GatewayCR.org**. We encourage you to share this information with your colleagues.

# Meet ... Emanuel F. Petricoin PhD



#### Professor, School of Systems Biology, George Mason University Co-Director, Center for Applied Proteomics and Molecular Medicine

Dr. Emanuel Petricoin is a molecular biologist leading a multidisciplinary team of scientists who invent and develop novel research technologies to explore mechanisms of disease related to protein structure and function. Two such technologies, the Reverse Phase Protein Array (RPPA) and Laser Capture Microdissection (LCM) are being utilized in the large multicenter ISPY-2 trial to identify predictive biomarkers of neoadjuvant therapeutics in women with Stage II/III breast cancer.

Building on the successful identification of five predictive biomarkers in a Gateway-funded Phase 1 study, Dr. Petricoin is expanding the search to another six with additional Gateway funding.

**Gateway:** Your research interest is personalized precision medicine, applying proteomic and genomic data to inform treatment strategies. What is/are the big question(s) you are exploring?

**Dr. Petricoin:** Proteins are the drug targets for nearly all targeted therapies that everyone is so excited about in the context of "personalized medicine". In fact, many targeted therapies actually modulate protein activity the phosphorylation state of the protein - not just the amount of protein present. These protein drug targets actually lie in signaling pathways that are often deranged in cancer - the protein "circuitry" of the cell. A very exciting ecosystem that has emerged from the molecular analysis of tumors is that each patient's tumor is very different when you look at which protein pathways are activated in each case. We have developed new technologies such as the Reverse Phase Protein Array that can map the activated signaling networks in each patient's individual tumor specimen. The big question we are exploring is what the clinical impact on patient outcomes is when this type of proteomic information is combined with genomic information for matching the correct therapy to the tumor molecular architecture.

**Gateway:** The Center for Applied Proteomics and Molecular Medicine at George Mason University is developing a novel class of nanotechnology for identifying protein biomarkers for early detection of cancer. Tell us about this work.

**Dr. Petricoin:** The ability to detect cancer at the earliest stages before it has grown and spread means that the amount of tumor, or even premalignant cells, is very small by definition. Moreover, the ability to develop assays and new diagnostic tests for early detection starts with monitoring a routinely obtained bio fluid such as blood or urine for the presence of protein biomarkers that arise from those emerging cancer cells. Consequently, there is an inherent analytical challenge to discover these new biomarkers that come

from microscopic quantities of cancer cells which are massively diluted in the large volume of blood or urine. The resultant concentration of any new cancer protein biomarker that can be used for early detection is exceedingly low, below the limit of detection for most discovery technologies.

We have developed a biomarker "harvesting" nanoparticle that is tuned with bait molecules that selectively concentrate and preserve low abundance protein biomarkers in seconds. These nanoparticles are magnetized and can be "fished" out of a blood or urine sample and concentrated as biomarker content for downstream detection. We have used this platform to identify new blood-borne biomarkers in early stage breast, ovarian, colorectal and other tumors and are validating these in prospective study sets.

# **Gateway:** What is the next frontier for precision oncology?

**Dr. Petricoin:** In my opinion, the next frontier is using advanced analytical data-mining methods such as artificial intelligence-based algorithms to uncover relationships between molecular profiling data – generated through combined proteomic, phosphoproteomic and genomic analysis of the tumor – and imaging data, both radiologic and pathology-based, that truly individualize treatment plans. This next frontier will see patient treatment plans based not on the site of origin of the tumor, like we do now, but on the unique patient-specific "persona".

# **Gateway:** Fill in the blank: My colleagues would be interested to know that I ...

**Dr. Petricoin:** ...worked at the U.S. Food and Drug Administration for 15 years as a senior investigator in the Center for Biologics Evaluation and Research. My time there gave me great insights into the regulatory environment of drug development, biomarker and diagnostic commercialization, and great appreciation for the urgency of getting safe and effective drugs and devices to the bedside for patient impact.

Gateway for Cancer Research welcomes Dr. Petricoin as the newest member of its Board of Directors, and thanks him for his dedication to the patients we serve.

# Managing Pain in Pancreatic Cancer

Gateway's funding model focuses on innovative, early stage patient-centered cancer research that improves treatment outcomes and restores quality of life. An example of this focus is a Phase II study underway with the support of Gateway, investigating an advanced pain management approach pioneered by researchers in Israel. This clinical trial is currently enrolling patients at leading cancer centers in the U.S. and abroad.

Patients with pancreatic cancer and other solid tumors in the upper abdomen often experience severe back pain in a "belt distribution." The pain is thought to originate in the celiac plexus, the nerves located behind the pancreas at the level of the 12th thoracic vertebrae.

Current pain management techniques, including opiate medications and nerve blocks, are insufficient and can significantly reduce patients' quality of life.

Gateway-funded researcher Yaacov Lawrence, MD, of Sheba Medical Center in Israel, recently completed a proof-of-concept pilot study to determine if delivering a single, high dose of radiation precisely targeted to the celiac plexus would benefit these patients. They demonstrated that celiac plexus radiosurgery is feasible and well-tolerated with minimal side effects, and it improved tolerability of prescribed therapies, helping to ensure that patients could continue treatment. Patients reported a considerable decrease in pain and improved quality of life. (See sidebar.)

Based on these findings, Dr. Lawrence is launching a Phase II multi-center clinical trial to determine if ablative radiosurgery decreases pain in patients with celiac-plexus pain syndrome, and to further assess the tolerability and side effects. Researchers will also explore the effects on patients' quality of life.

Dr. Lawrence seeks to enroll 100 patients in the Phase II study. In addition to the main study site at Sheba Medical Center in Ramat Gan, Israel, participating sites include:

- Mount Sinai Hospital, New York, NY
- Ohio State University, Columbus, OH
- Princess Margaret Cancer Center, Toronto, Canada
- Assuta Medical Center, Tel Aviv, Israel
- Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
- Instituto Portugues de Oncologia do Porto Francisco Gentil, Porto, Portugal

To refer a patient or explore opportunities for collaboration, please contact Dr. Lawrence at yaacovla@gmail.com.



#### THE PATIENT'S VOICE ...

"My mom participated in your clinical trial. It was a huge success and her pain is now 100 percent gone. I am so very thankful because she has not had to be on any pain meds since the procedure. Previously, she just slept all the time and we could not hold a conversation. Thank you for allowing us to have more conversations. My family and I will always cherish these last few conversations and we will always be grateful to you and your team for giving us that gift."

> - Daughter of patient treated at Ohio State University

"I am so grateful and feel so fortunate to be part of the radiation therapy against pancreatic cancer pain. I am almost pain-free and life is very bearable and good. I became a great-grandmother again this week and I have a grandchild's wedding in a week and a half where I will dance (hopefully). All normal and wonderful things. Keep up the brilliant work and many, many thanks."

- JG, Jerusalem

| An          | nerican Society of<br>Hematology | <b>ASH Annual Meeting and Exposition</b><br>December 5 – 8, 2020 – Virtual  |  |
|-------------|----------------------------------|---|--|
|             | THE NEWS                         |   |  |
|             | ASCO Connection                  | The Return of the Physician House Call: Caring in Bytes and Pieces<br>September 17, 2020  |  |
|             | Nature Medicine                  | Scientists, keep an open line of communication with the public<br>October 5, 2020   |  |
|             | ASCO Connection                  | Taking a Stand: A Conversation About Health Equity<br>October 29, 2020  |  |
| Gateway for | r Cancer Research                | <b>\$1.5 Million Gateway Discovery Grant to Fund Clinical Cancer Research Addressing Health Disparities</b><br>November 5, 2020 |  |



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