

CONQUEST 2021

A Report on the Maryland Cigarette Restitution Fund

Unquestionably, the last year was framed by the COVID-19 global pandemic, and the human and financial toll it has taken on our state. However, amidst these challenges, there were triumphs. CRF investigators were among the Johns Hopkins experts who led efforts to understand and contain this novel virus. Around the country, and here at home, cancer experts sprang into action, rapidly launching projects that advanced testing and proposed life-saving therapies.

During this time of pandemic, we cared for many patients transferred from other hospitals and clinics throughout the state who could not care for COVID-positive patients. We worked collaboratively with Maryland elected officials and our colleagues at the University of Maryland to construct a field hospital to address the additional strain the virus placed on Maryland hospitals. We deployed COVID guidelines that were adapted by hospitals across the nation.

Of course, we also remained stalwart participants in our shared mission to combat cancer in Maryland, building upon our CRF infrastructure to expand collaborations and services.

We are aware that there are more than financial challenges that lay ahead. The challenges of missed cancer screenings are on the rise due to the pandemic. As is often the case, the most vulnerable of our state—the poor and disenfranchised—suffer the most. As you will read (see pages 3-5), we are engaging our partners in the community, state and local health departments and other national thought leaders in cancer health disparities research, working together to eliminate disparities and save lives through screening and early detection.

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Combatting COVID-19

Maryland Cigarette Restitution Fund investigators were among the Johns Hopkins scientists and clinicians who helped the state address the COVID-19 pandemic.



Protecting Patients While Continuing Care: The Kimmel Cancer Center opened a Curbside Shot Clinic—a drive-up treatment delivery system—for outpatients and a special Urgent Care Bio Clinic for cancer patients infected with the coronavirus.

Testing Kits: A trained team made approximately 30,000 COVID-19 testing kits in a Kimmel Cancer Center lab uniquely outfitted to meet special quality control standards required for manufacturing pharmaceutical products. Research laboratories throughout the Cancer Center donated supplies needed to complete the kits.

Preventing Lethal Outcomes: Experts worked to identify which COVID-19 patients would need medical interventions to save their lives versus those likely to recover naturally. Although most people

recover from COVID-19, some patients take a dramatic downhill course that is often lethal. A new analysis of white blood cells is being developed to identify individuals who need intervention at an earlier stage to prevent the acceleration of their COVID-19 disease.

Defining T Cell Responses: Researchers adapted a new technology called MANAFEST — originally developed to analyze cancer-specific T cell responses in immunotherapy patients — to assess T cell responses in COVID-19 patients who are experiencing mild symptoms, respiratory compromise or receiving a COVID-19 experimental vaccine. T cells are key to generating an individual's protective immunity against subsequent infections. Since it is almost certain that the coronavirus will reappear in successive waves, defining who has developed protective immunity to the virus is critical.

COVID Therapy explored: Researchers found that the drug prazosin, an alpha blocker most commonly used to treat high blood pressure and prostate enlargement, could prevent an inflammatory process called cytokine storm syndrome, which is often associated with an overproduction of immune cells that causes lung inflammation and serious respiratory problems. The cytokine storm syndrome disproportionately affects older adults with underlying health conditions and is associated with severity and death in COVID-19.



Race, Healthcare Disparities, and Equity in Care



Eliminating race and geographic disparities are key to making progress against cancer in Maryland. From collaborating on national efforts to combat disparities to assessing, identifying and addressing screening deficiencies and trends in Maryland, CRF investigators are taking action. The impact of CRF support is broadened as investigators earn additional funding through federal grants and private donations to address specific health disparities in Maryland.

Podcast on Health Disparities: <u>Listen to CRF investigators</u> William Nelson, M.D., Ph.D., Director of the Kimmel Cancer Center, Otis Brawley, M.D., Director of Community Outreach and Engagement, and Dina Lansey, M.S.N., Assistant Director of Diversity and Inclusion in Clinical Research, discuss efforts to address health disparities in Maryland.



Controlling Colon Cancer: African Americans die disproportionately from colon cancer. CRF researcher Norma Kanarek, M.P.H., Ph.D., identified a higher death rate among African American men living along the I-95 corridor from Prince Georges County to Baltimore. Collaborating with CRF investigator and Kimmel Cancer Center Community Outreach and Engagement Director Otis Brawley, M.D., Bloomberg Distinguished Professor, the Maryland Department of Health Center for Cancer Prevention and Control, and Radio One, they initiated the DontDelay.Today campaign for colon cancer prevention and early detection among African Americans. The initiation, promoted by Radio One, directly addresses a problem identified in the community through the CRF and provides information on the importance of colon cancer screening and connects people to no-cost screening and information on healthy diet, habits and exercise.

Dialog on Race in Medicine: The Johns Hopkins Kimmel Cancer Center presented a three-part virtual series addressing access to cancer care, social determinants of health, and ethnic composition of cancer physicians. Kimmel Cancer Center Director William Nelson, M.D., Ph.D., Akila Viswanathan, M.D.,



M.P.H., Director of Radiation Oncology and Molecular Radiation Sciences, Otis Brawley, M.D., Director of Community Outreach and Engagement, and Ashwani Rajput, M.D., Medical Director of the Kimmel Cancer Center in the Washington, D.C., region led discussions and an interactive exchange on urgent issues of race in medicine.

Conversations in Healthcare Equity: Otis Brawley, M.D., also initiated conversations with faculty at other Baltimore universities, including, Loyola University and Morgan State University around reconciliation, peacebuilding and social change to improve healthcare disparities. <u>Listen</u> to Dr. Brawley's podcast "Cancer Disparities."

Smoking Cessation: Panagis Galiatsatos, M.D., M.H.S., hosts a smoking cessation clinic at Bayview and worked with the American Thoracic Society to make recommendations for treatment of nicotine addiction. Recommendations include the drug varenicline, now available over the counter. Galiatsatos also trained community health care workers who are making outreach to public housing residents to provide smoking cessation services.

National Report on Cancer Disparities: The American Association for Cancer Research released its inaugural Cancer Disparities Progress Report described as a collective effort of a number of the world's foremost thought leaders in cancer health disparities research. **William Nelson, M.D., Ph.D.**, Director of the Kimmel Cancer Center contributed to this first-of-its-kind report as a member of the Steering Committee and young faculty member and CRF investigator Jelani Zarif, also contributed. The report was presented to the U.S. Congress in a virtual ceremony.



"Many cancer disparity gaps have persisted for decades. We hope this report will serve as a guide for how research questions can help address & close these gaps. -- Jelani Zarif, Ph.D., Maryland Cigarette Restitution Fund investigator and contributor to the inaugural report.

Minority Health Grant: Kimmel Cancer Center experts, in collaboration with Howard University, and Bloomberg School of Public Health Social Determinants of Health program faculty members applied for a National Cancer Institute Specialized Programs of Research

Excellence (SPORE) grant in minority health to address disparities in cancer incidence, prevalence, mortality, survivorship, and burden of cancer among racial/ethnic minority populations. The proposed research will be led by CRF investigators, including Otis Brawley, M.D., and will leverage CRF-supported research to expand the scope of health disparities initiatives.

Progress Against Prostate Cancer: Prostate cancer is a CRF-targeted cancer with death rates that disproportionately affect African American men in Maryland, particularly Baltimore City. Building upon CRF-supporting and other Kimmel Cancer Center prostate cancer research, **William Nelson, M.D, Ph.D.**, applied for a grant from the Department of Defense to further explore an aggressive subtype of prostate cancer he uncovered that is more common among African American men.

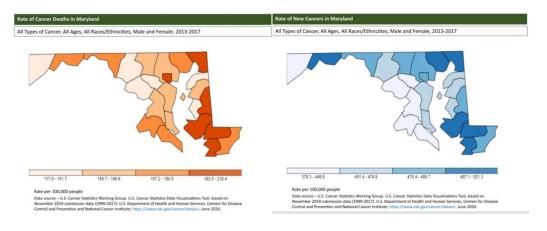
Maryland Declines in Cancer Death Race Differences

Maryland and the U.S. are seeing similar declines in cancer mortality race differences, with Maryland surpassing the U.S.

TABLE 1 Absolute and Re Changes, Maryl		•		ortality	Rates Fr	om 1990 to	2015 an	d Black-	White Diff	erences	in Those	9	
	Maryland						United States						
		Rate			Black-White Rate Difference			Rate			Black-White Rate Difference		
	1990	2015	Change	1990	2015	Change	1990	2015	Change	1990	2015	Change	
All cancers	241.7	155.3	-47%	85.9	25.7	-70%	214.9	158.7	-26%	68.9	21.6	-69%	
Seven targeted	140.7	76.9	-45%	47.4	16.7	-65%	125.3	79.6	-27%	41.6	15.4	-63%	

Understanding Our Catchment Area to Address Specific Needs

Despite the monumental successes achieved by the State of Maryland over the past 30 years, pockets of cancer health disparities remain (see figure) and we are intensively investing CRF funds to uncover these disparities and develop effective interventions. In addition to Baltimore City, some of Maryland's rural areas are highest in both cancer deaths and new cases. The maps show the counties with the greatest challenges in cancer deaths and new cancer cases, so that we can guide and direct research and outreach to those areas. It also shows counties that are improving, allowing us to monitor progress and identify successful strategies.



CRF-Supported Research Making News

Precision Cancer Medicine: Victor Velculescu, M.D., Ph.D., a CRF faculty recruitment grant recipient, is overseeing a precision medicine genomics portal that includes over 7,000 patients, containing genetic data, tumor characteristics, basic demographic information, and overall survival. The data portal, which will be directed by CRF faculty recruitment grant investigator Alex Baras, M.D., Ph.D., allows users to create complex custom analyses based on clinical, tissue sample, and genomic features, and perform these through an interactive web data viewer, providing a unique avenue for further research in cancer genomics and precision medicine. Among its many capabilities, it can help advance progress against cancer in underserved and minority populations.

First Study of Multicancer Blood Test: Results from a first-of-its-kind study of the CancerSEEK multicancer blood test in more than 9,900 women with no evidence or history of cancer showed the liquid biopsy test efficiently detected 26 undiagnosed cancers, enabling potentially curative treatment. Cancers detected by the blood test were most often localized by a follow-up diagnostic PET-CT. Twelve of the cancers detected by the blood test were able to be surgically removed. The study represents the first time any liquid biopsy blood test was used clinically to screen for cancer in a population without previously detected cancer for the purpose of diagnosis and treatment with the intent to cure cancer. Specific plans to ensure the test is deployed, once approved, to underserved communities. This testing is especially important because cancers are often not found until they have advanced to a late, less curable stage. One of the key investigators was also a CRF research grant recipient.

Remote Coaching and Healthy Weight Loss: A telephone-coaching and web-based weight loss plan, called the POWER-remote intervention for overweight and obese breast cancer survivors, helped half of them lose 5% or more of their body weight after six months — and to keep it off for 12 months. Obesity is a major risk factor for many cancers, including breast cancer, the researchers note. In addition, most women gain weight following a breast cancer diagnosis, which has been associated with a 1.5-fold increased risk of breast cancer recurrence and death. The first clinical trial was funded by a CRF research grant at Johns Hopkins.

Healthy Weight and Sleep for Survivors: A study to promote both healthy sleep and healthy weight in cancer survivors. Called COIN, for Cancer Obesity/Overweight Insomnia, the study targets sleep, a critical and neglected component of weight loss treatment. Over one-half of breast cancer patients struggle with excess weight, and this adversely impacts quality of life and may increase the risk of the cancer coming back by 40% to 50% and the risk of dying from their cancer by 50% to 60%. In addition, 20% to 70% of cancer patients are sleep deprived, and this alone has been linked to poor outcomes.

Pioneering Drug Approval: The U.S. Food and Drug Administration (FDA) approved the anti-PD-1 checkpoint blocker pembrolizumab (Keytruda) for first-line treatment of patients with

inoperable, advanced colorectal cancer that has spread to other places of the body and has a biomarker called mismatch repair deficiency. This marks the first immunotherapy approved for this patient population as a first-line treatment that can be given to patients without traditional chemotherapy. The approval developed from pioneering science funded, in part, by the CRF, revealed mismatch repair deficiency as a glitch in a "spell check"- like feature that leads to defects in DNA, creating abnormalities in tumors that the immune system recognizes. The finding led to the FDA's historic 2017 approval of pembrolizumab for all cancers that have mismatch repair deficiency, making it the first-ever drug approval not tied to a specific cancer type. The latest FDA approval for colorectal cancer builds on that original discovery. CRF investigators Nilofer Azad, M.D., and Robert Anders, M.D., Ph.D., were part of the research team and clinical study that led to the approvals.

Chemotherapy/Immunotherapy Combo for Mesothelioma: A clinical study, called PrE0505, evaluated an immunotherapy-plus-chemotherapy combination for inoperable malignant pleural mesothelioma, a rare and aggressive cancer of the protective lining of the lungs, or pleura, often caused by exposure to asbestos. Patients were treated with the anti-PD-L1 immunotherapy drug durvalumab in combination with the anticancer chemotherapies cisplatin and pemetrexed as a first treatment. The chemo-immunotherapy combination improved overall survival from historical expected survival of 12 months with chemotherapy alone to 20.4 months with the chemo-immunotherapy combination. This is the first study to show survival exceeding 20 months for patients with inoperable mesothelioma. CRF investigators **Julie Brahmer, M.D.**, and **Valsamo "Elsa" Anagnostou, M.D., Ph.D.**, were part of the research team.

Crosstalk Among Tumor Cells and Immune Cells: Researchers used machine learning tools (artificial intelligence) and comprehensive studies of the genomes and transcriptome (RNA produced by genes) of cancer cells and immune T cells to study the interplay among cancer cells and immune cells. Their goal is development of an integrated molecular biomarker to help physicians identify patients most likely to respond to immunotherapy. CRF investigator Valsamo "Elsa" Anagnostou, M.D., Ph.D., led this study.

Researchers Develop Ultrasensitive Blood Test to Predict Recurrence of Gastric Cancers: Researchers reported on a blood test that can predict recurrence of gastric cancer in patients after surgery. Investigators analyzed blood samples from 50 patients with gastric cancer who participated in the CRITICS trial, a phase III, randomized controlled study of chemotherapy given at about the time of surgery. They performed deep sequencing of both circulating cell-free DNA and of white blood cells to look for mutations and predict cancer recurrence within nine weeks following preoperative treatment and surgery. Patients who did not have mutations in the blood after surgery were all cured of cancer, while patients who had mutations in the blood typically recurred. CRF investigator **Victor Velculescu**, **Ph.D.**, led this study.

PGDx Milestone: Personal Genome Diagnostics, a company started by CRF investigators, reached a key milestone in its effort to make genomic profiling of cancer available to patients and oncologists at the local level — and it's the first to do so for a product of its kind. The Canton-based company received U.S. Food and Drug Administration clearance for its diagnostic kit, called *PGDx elio tissue complete*. Combining chemistry performed on a DNA sample and software that automates the data analysis process, the test can perform genomic

profiling of a patient's tissue sample in molecular labs in a hospital. This can open up access to a level of genomic analysis that currently requires Maryland citizens and hospitals to send samples out to a faraway lab.

The Dangers of Smoking/E-Cigarettes: Pulmonologist and CRF investigator Panagis Galiatsatos, M.D., M.H.S., has focused his career or understanding the biological and social causes of tobacco use and nicotine addiction. His research revealed specific smoking phenotypes, or genetic characteristics that can impact the severity of addiction. For example, those predisposed to slower metabolism of nicotine will find it easier to quit. He also studies social factors, such as peer groups, and how they influence smoking, vaping and quitting success. He also warns of the dangers of e-cigarettes, which can result in more severe nicotine addiction and contribute to several disease syndromes. Galiatsatos Creates individualized plans, including behavioral and medical interventions based on the types of cigarettes a person smoked and the amount of nicotine they provided, to help patients stop smoking. He is working to develop similar approaches to help people quit e-cigarettes, which he says are more addictive than cigarettes and are implicated in several disease syndromes, including reactive airway disease, asthma, and microbacterial infections. Listen to his podcast for more information on the dangers of smoking, vaping and nicotine addiction.

2021 AWARDS

FY21 Awards \$2,340,000

Grants:	All	New	FY Target
Translational Research	17	7	15
Faculty Recruitment	9	0	9
Faculty Retention	0	0	0
TOTAL	26		24

Anna Beavis, M.D., M.P.H.: Addressing rising obesity and gynecologic cancer risks through primary prevention: a risk prediction model to guide screening for endometrial hyperplasia and cancer in obese women **FACULTY RECRUITMENT, CONTINUATION**

Otis Brawley, M.D.: Reduction of the cancer burden in the SKCCC catchment area through disparities elimination **FACULTY RECRUITMENT, CONTINUATION**

Otis Brawley, M.D., and Norma Kanarek, Ph.D.: Engaging the Johns Hopkins Health System in Research to Reduce the Burden of Cancer in the SKCCC Catchment Area TRANSLATIONAL RESEARCH, NEW

Robert Brown, M.D.: Morbid Obesity, Bariatric Surgery, and Proteomic Measurements o Reduced Risk of Liver Cancer **TRANSLATIONAL RESEARCH, NEW**

Namandje N. Bumpus, Ph.D.: Development of a Novel Class of Bim Activators as Chemotherapeutic Agent TRANSLATIONAL RESEARCH, CONTINUATION

Geentanjali Chander, M.D., M.P.H., and Heidi E. Hutton, Ph.D.: Pilot RCT of an avatar delivered smoking cessation intervention for low income hospitalized smokers in Baltimore City TRANSLATIONAL RESEARCH, CONTINUATION

Alan D. Friedman, Ph.D.: EGFR-Targeted Activated Myeloid Cells as a Novel Immunotherapy for Lung Cancer **TRANSLATIONAL RESEARCH, NEW**

Panagis Galiatsatos, M.D.: Tobacco Free Community Initiative TRANSLATIONAL RESEARCH, CONTINUATION

Jacky Jennings, Ph.D.: Improving Patient Care and Population Health Using Patient-Reported Outcomes: Developing a PRO **TRANSLATIONAL RESEARCH, NEW**

Norma Kanarek, M.P.H., Ph.D.: Understanding Smoking Behaviors in Baltimore City TRANSLATIONAL RESEARCH, CONTINUATION

Vincent Lam, M.D.: Longitudinal Circulating Tumor DNA Profiling of Resected Esophageal Cancer for Early Recurrence Detection Characterization of Tumor Clonal Evolution. **FACULTY RECRUITMENT, CONTINUATION**

Dina Lansey, M.S.N.: Identifying Barriers to Therapeutic Clinical Trial Participation Using Clinical Trial Candidate Data **TRANSLATIONAL RESEARCH, NEW**

Catherine Handy Marshall, M.D., M.P.H.: Modifiable risk factors in cancer FACULTY RECRUITMENT, CONTINUATION

Elizabeth Platz, M.P.H., Sc.D.: Cancer Prevention and Control Biostatistics Core for Research and Proposals TRANSLATIONAL RESEARCH, CONTINUATION

Elizabeth Platz, M.P.H., Sc.D.: Periodontal Pathogens and Risk of Cancer in a Cohort that Includes Marylanders From Washington County TRANSLATIONAL RESEARCH, NEW

Karisa Schreck, M.D., Ph.D: *Targeting SHP2-dependent adaptive resistance to RAF inhibition in BRAF-mutated glioma.* **FACULTY RECRUITMENT, CONTINUATION**

Jennifer Sheng, M.D.: An adaptive weight loss program in overweight or obese breast cancer survivors FACULTY RECRUITMENT, CONTINUATION

Tanguy Siewert, M.D.: A Novel Model System to Optimize Immunotherapy for Oral Cancer Patients Using a Histoculture-Bioreactor System **FACULTY RECRUITMENT, CONTINUATION**

Fenna Sille, Ph.D.: Investigating How Arsenic from Cigarette Smoke and Drinking Water Exposures Cause Lung Cancer **TRANSLATIONAL RESEARCH, NEW**

Claire Snyder, Ph.D.: PRO-cision Medicine: Refining a Patient-Centered Strategy for Cancer Care TRANSLATIONAL RESEARCH, CONTINUATION

Jessica Tao, M.D.: Circulating Tumor DNA as a Screening Biomarker for Aggressive Breast Cancer **FACULTY RECRUITMENT, CONTINUATION**

Kala Visvanathan, M.D.: Using Artificial Intelligence (AI) to address the clinical need for timely high-quality germline testing on cancer patients TRANSLATIONAL RESEARCH, CONTINUATION

Jessica Yeh, Ph.D.: Behavioral Weight Loss for Overweight or Obese Cancer Survivors in Maryland: ASPIRE Study **TRANSLATIONAL RESEARCH, CONTINUATION**

James Zabora, Sc.D.: Evaluation of the Johns Hopkins Center to Reduce Cancer Disparities' Community Advisory Groups (CAGs)-Part II TRANSLATIONAL RESEARCH, CONTINUATION

Cynthia Zahnow, Ph.D.: Alcohol exposure alters the epigenome to increase breast cancer TRANSLATIONAL RESEARCH, CONTINUATION

Jelani Zarif, M.D.: Targeting M2-Tumor Associated Macrophages (M2-TAMs) in Prostate Cancer **FACULTY RECRUITMENT, CONTINUATION**