



JOHNS HOPKINS CONQUEST 2018

A Report on the Maryland Cigarette Restitution Fund

Cancer research and medicine has long benefited from a team-based approach. In many ways, this strategy of engaging all stakeholders to develop solutions to shared problems has been a model for how progress can be made against the most difficult challenges.

This spirit of collaboration—the knowledge that working together amplifies benefit—led to the Johns Hopkins, federal, and state partnership that brought a cancer center to Johns Hopkins in 1973. This same vision was in play in 2001, when Maryland’s governor and General Assembly established the Cigarette Restitution Fund (CRF) and used it to combat cancer on every front.

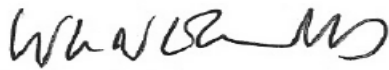
Advances do not occur in a vacuum. When we report progress against a specific cancer or in an area of research supported by the CRF, these discoveries and accomplishments have far-reaching impact well beyond any single cancer or research project. There is a ripple effect extending to all scientific and medical disciplines combating cancer.

The success of the CRF reflects these advances as well as the power of staying the course and maintaining an investment in cancer research in good economic times and in difficult ones.

A recent groundbreaking advance supported in part by the CRF was nearly 25 years in the making. A 1994 Cancer Center discovery of mutations in a set of DNA-repairing genes was central to the historic FDA approval just a few months ago of the immunotherapy pembrolizumab (Keytruda). Both the identification of the repair genes and their link to immunotherapy responses were homegrown discoveries made by researchers in our Johns Hopkins Kimmel Cancer Center. It was the first time ever that a drug was FDA-approved for cancer based on disease genetics rather than where in the body the cancer occurred. It happened because cancer genetics and cancer immunology experts worked together, persevered despite difficult and complicated scientific obstacles, and were supported throughout by a variety of sources, including the Maryland CRF.

Although not all of the researchers involved in this project were CRF funded, our CRF support contributed to this monumental advance. This approach accomplishes our CRF goals and so much more.

Just as we have learned that we cannot silo cancer research by cancer type, we also recognize that we cannot silo progress either—they are all interrelated. Everything the CRF touches has impact well beyond that individual researcher, cancer type or laboratory discovery. It is the building of ideas and cross-pollination of discovery among many areas of expertise and specialties that result in the progress Maryland has made against cancer. The CRF is a stakeholder. Each Kimmel Cancer Center success story of patient survival against all odds, each story about our research advances against cancer and each story of new companies launched to bring better diagnostic technologies and cancer drugs to market is a CRF success story.

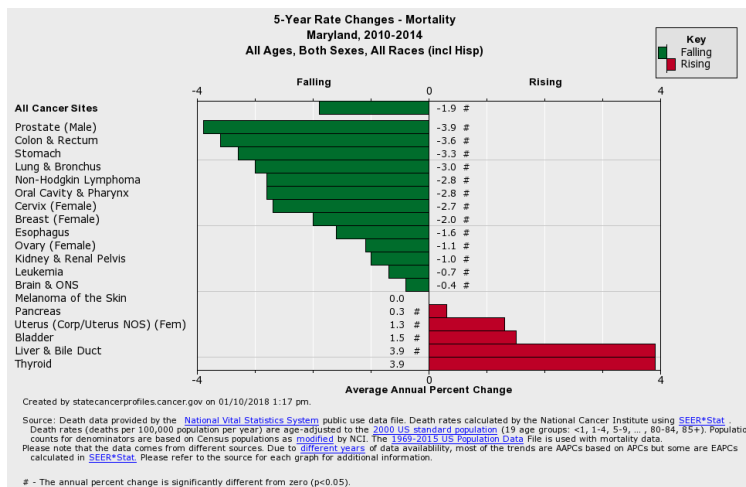


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FAVORABLE TRENDS CONTINUE IN MARYLAND



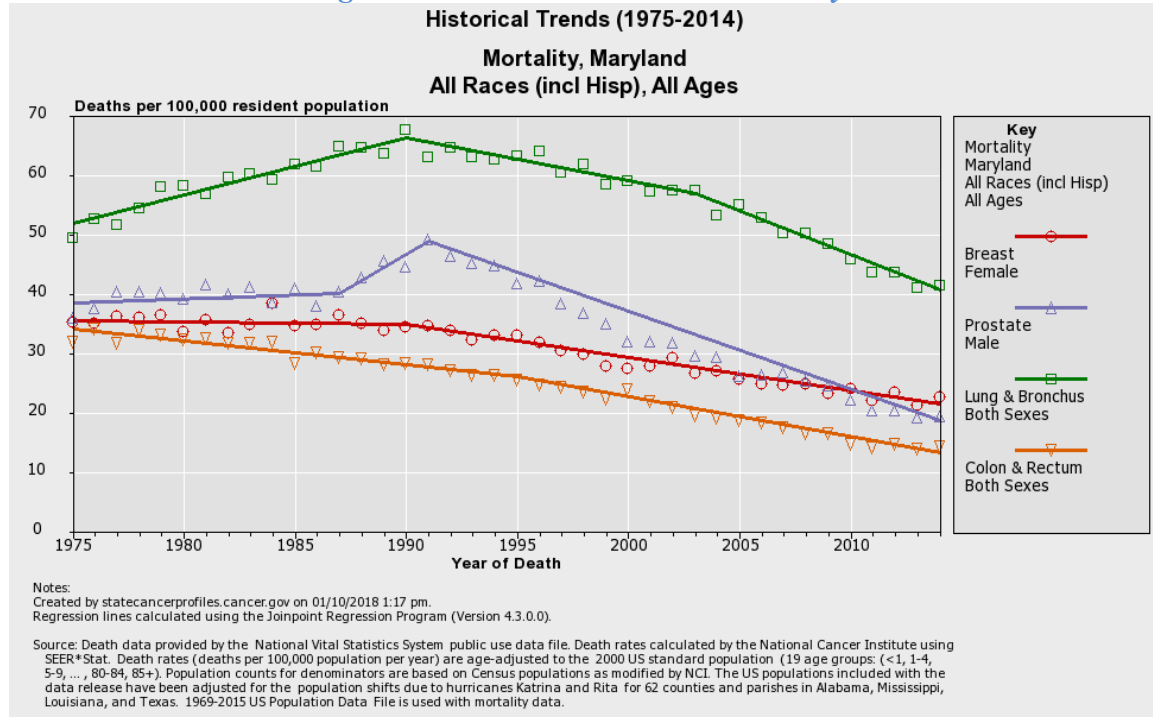
Cancer deaths continue to decline in Maryland. At the same time, new efforts are directed at cancers with rising incidence and death rates. The Cancer Center’s Bloomberg-Kimmel Institute for Cancer Immunotherapy is providing promising new immunotherapies for pancreatic cancer, melanoma skin cancer and rare GI cancers, such as liver and bile duct cancer, which are

on the rise. Immunotherapy is one of the most exciting new advances in cancer medicine, and Johns Hopkins is on the leading edge of these discoveries. Our Greenberg Bladder Cancer Institute is aimed at understanding, preventing and curing bladder cancer, which is also among the cancers trending upward in our state.

The Kimmel Cancer Center and Maryland

Working together to make progress

Cancer death rates among all races continue to decline in Maryland.



Notable Numbers:

- Approximately **36 percent of Kimmel Cancer Center patients are from Baltimore City, Maryland.**
- **Maryland ranks 31st in cancer incidence** among all states and Washington, D.C. Maryland is below the median incidence rate for five of the seven CRF-targeted cancers: prostate is third, breast is 17th, melanoma is 27th, colorectal is 30th, lung/bronchus is 36th, cervix is 40th, and oral cavity and pharynx are 43rd. Despite the greatest progress in prostate cancer incidence through better screening and targeted treatment, breast cancer remains an important site of diagnosis for women and incidence has remained virtually unchanged in the U.S. and Maryland.
- **Maryland ranks 30th** among states and Washington, D.C., **for cancer deaths** (2015 death rates).
- More than **16 percent of Maryland cancers are diagnosed at the Kimmel Cancer Center** (2014).
- All **CRF-targeted cancers**, except for melanoma skin cancer, **have declined by 2 to 4 percent per year.**
- **Maryland cancer deaths** overall have declined **by 2 percent annually.**

Notable News:

Historic Cancer Drug Approval: “It’s not often that a single institution discovers the cause of a disease and the treatment for it,” says Bert Vogelstein, M.D., whose research team, including CRF investigators **Robert Anders, M.D., Ph.D.**, **Nilofer Azad, M.D.** and **James Echleman, M.D., Ph.D.**, led to the historic approval of the immunotherapy drug pembrolizumab (Keytruda). The drug was approved for all cancers with a DNA repair defect called mismatch repair deficiency. It is the first-ever drug approval not tied to a specific cancer type. The research to identify the gene defect and the clinical trial that led to the drug approval all occurred in the Kimmel Cancer Center.

QUICK FACTS

86

patients with mismatch repair deficiency tumors

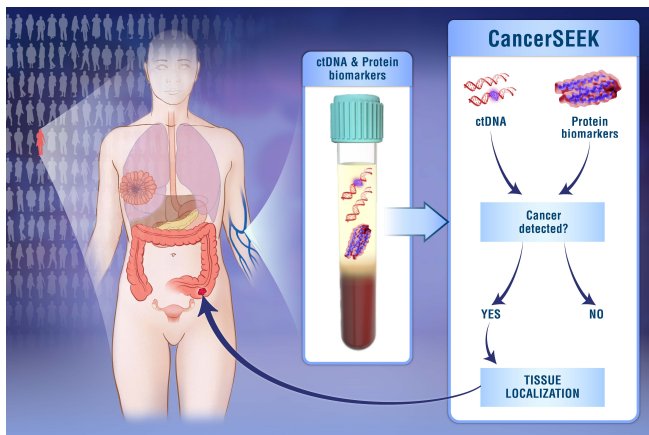
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different cancer types represented

21%

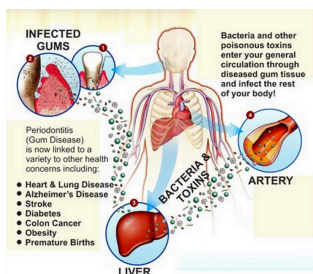
had their tumors disappear completely; more than 50% had their tumors shrink

Science
AAAS



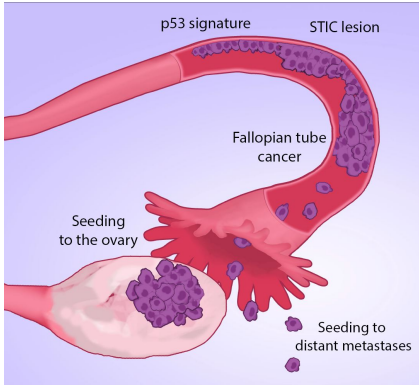
Cancer Test: Kimmel Cancer Center researchers, including CRF investigator **Cristian Tomasetti, Ph.D.**, developed a single blood test that screens for eight common cancer types and helps identify the location of the cancer. The test, called CancerSEEK, is a unique blood test that simultaneously evaluates levels of eight cancer proteins and the presence of cancer gene mutations from circulating

DNA in the blood. The test is aimed at screening for eight common cancer types that account for more than 60 percent of cancer deaths in the U.S. Five of the cancers covered by the test currently have no screening test.



Gum Disease Linked to Cancer: Data collected during a long-term health study provide evidence for a link between increased risk of lung and colon cancers in individuals with advanced gum disease, which is caused by bacterial infection that damages the soft tissue and bone that support the teeth. “It may be that the bacteria that cause periodontal disease go from the mouth directly into the lungs or from the mouth into the colon,” says **Elizabeth Platz, Sc.D.**, a CRF investigator and

cancer prevention and control expert. “If they were to cause an inflammatory response, that could increase the risk of cancer forming.”



The Roots of Ovarian Cancer: Some scientists have suspected that the most common form of ovarian cancer may originate in the fallopian tubes, the thin fibrous tunnels that connect the ovaries to the uterus. Now results of a study led by **CRF investigator Victor Velculescu, M.D., Ph.D.**, suggest that the genomic roots of many ovarian tumors may indeed arise in the fallopian tubes, potentially providing insights into the origin of ovarian cancer and suggesting new ways for prevention and intervention of this disease.

Mutations and Immunotherapy: The “mutational burden,” or the number of mutations present in a tumor’s DNA, is a good predictor of whether that cancer type will respond to a class of cancer immunotherapy drugs known as checkpoint inhibitors, a new study led by **CRF investigator Mark Yarchoan, M.D.**, found. He notes that these findings could help guide clinical trials to test checkpoint inhibitors on cancer types for which these drugs haven’t yet been tried. Future studies might also focus on finding ways to prompt cancers with low mutational burdens to behave like those with higher mutational burdens so that they will respond better to these therapies.

Research Brings Improved Health to Maryland Citizens and Economy

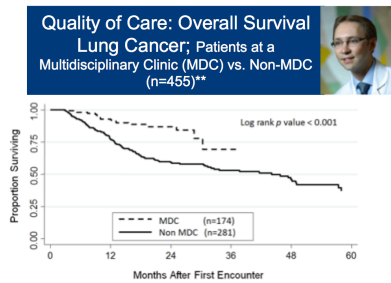
“Johns Hopkins has turned Baltimore into quite a liquid biopsy biotech hub.”—Megan Molteni, reporter for Wired

Kimball Cancer Center research led to the Maryland-based biotech startups Personal Genome Diagnostics (PGDx) and PapGene, Inc. Victor Velculescu, M.D., Ph.D., a PGDx founder and some founders of PapGene received CRF support.

Maryland Center for Cell Therapy Manufacturing



Personalized Cell Therapy: A new joint venture brings more biotech industry to Maryland. The new undertaking is based on the work of Ivan Borrello, M.D. His success using cells known as marrow-infiltrating cells (MILs) to treat multiple myeloma, a currently incurable blood cancer, led to expansion of the therapy to treat lung, esophageal, HPV-positive head and neck, and prostate cancers. The treatment involves collecting these special immune cells from a patient’s bone marrow, expanding their numbers and then giving them back to the patient through an intravenous infusion, where they seek out and destroy cancer cells.



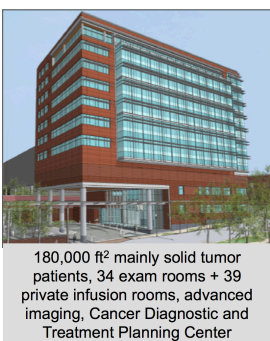
Precision Multispecialty Medicine: The Kimmel Cancer Center’s unique multispecialty precision medicine clinics save lives! Patients with lung, pancreatic, prostate and other cancers live longer when seen in these specialty clinics.



New Cancer Drug: CRF investigator Marikki Laiho, M.D., Ph.D., developed a drug that targets an enzyme called RNA polymerase I, or Pol I, which is implicated in many forms of cancer. It became the first project for Bluefield Innovations, a collaboration between Deerfield Management and The Johns Hopkins University to catalyze early-stage therapeutic development. Laiho’s research indicates that her drug could interfere with this pathway and kill cancer cells without causing harm to normal cells.



Johns Hopkins as a GAITWAY: The ability to decipher the data gene sequencing produces to determine which are important to the care of cancer patients is a complex science. Genetic Alteration in Tumors with Actionable Yields, or GAITWAY, is a board made up of about a dozen Johns Hopkins experts, including oncologists, geneticists, molecular pathologists, genetic counselors and a patient advocate. They review cancer gene sequencing reports from Johns Hopkins colleagues, community physicians, and Johns Hopkins partners and affiliates, such as the Allegheny Health Network and Johns Hopkins Singapore, to determine if they contain any actionable targets—gene alterations that have corresponding drugs that work against them.



Skip Viragh Outpatient Cancer Building: As more and more cancer care is provided in the outpatient setting, and with Marylanders representing 62% of patients treated at the Kimmel Cancer Center, the new Skip Viragh Outpatient Cancer Building fills a critical unmet need. The state-of-the art outpatient facility opens in spring 2018. Features include a real-time location system that displays the locations of patients and helps automate workflows, optimize operations and improve patient experiences. Among its many outpatient cancer services, the new building will house the multispecialty cancer clinics, immunotherapy clinic and the Under Armour Breast Health Innovation Center.



Bloomberg~Kimmel Institute for Cancer Immunotherapy: The Kimmel Cancer Center is home to one of the first specialty centers focused on immunotherapy research and treatment. Immunotherapies are treatments that activate the immune system against cancer. “The BKI is extremely exciting from a scientific perspective and in terms of clinical impact, I think a lot of institutions will be watching. It has the potential to be a role model for similar efforts at other places,” says Dario Vignali, chair of cancer immunology at the University of Pittsburgh and the BKI’s advisory board



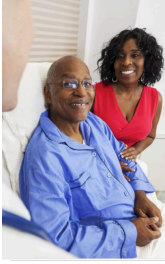
Young Adults Cancer Program: Overall cure rates among pediatric cancer patients are significantly higher than the rates for adult cancer patients for acute lymphocytic leukemia and a number of other cancers. At Johns Hopkins, a growing number of young adults, up to age 25, are referred by adult oncologists for treatment in pediatric oncology. The program was championed by pediatric oncologist and leading bone marrow transplant expert Kenneth Cooke, M.D. “A young adult’s organ systems are more like a 10-year-old’s than a 65-year-old’s. The therapy that we give in pediatric oncology is more intense. Young adults can tolerate it, and as a result, cure rates are higher,” says Cooke. Our experts focus less on age and more on making sure patients receive the right treatment for their cancer type and stage of life. The age range can be modified depending on the availability of cutting edge clinical trials, leaving plenty of room for pediatricians and adult doctors to work together and recommend patients to each other.

More on how Kimmel Cancer Center Pediatric Oncology is making Maryland a leader in childhood cancer research and treatment:



- We are ranked #6 nationally on *U.S. News & World Report’s* Best Children’s Hospitals for Pediatric Cancer list, and the Kimmel Cancer Center is also ranked #6 nationally.
- The Johns Hopkins Hospital is the nation’s top-ranked hospital combined for both adult and pediatric care in the *U.S. News & World Report* Best Hospitals list.
- Pediatric cancer experts receive training through a joint pediatric oncology/hematology training program with the National Institutes of Health.
- It is a national referral center for stem cell and bone marrow transplantation. Kimmel Cancer Center-pioneered half-identical bone marrow transplants make it possible to do transplants for all patients, even those who do not have perfectly matching donors. **African-Americans, Hispanics and other minorities, who have historically been excluded from transplants because of the inability to find matching donors, now have the highest accrual to bone marrow transplant clinical trials in the history of the therapy.**

Kimmel in the Community: Reducing Cancer Disparities



The gap in cancer death rates between African-American and white Marylanders has **narrowed by 60 percent** since 2001, a number that far exceeds the national average.

The number of **minority patients** from Maryland treated at the Kimmel Cancer Center has **increased from 985 in 2010 to 1,255** in 2015.

Prostate cancer **death rates among African-Americans in Maryland have declined by 40 percent**, and **race disparities in all cancer death rates have narrowed by 40 percent**.

CRF investigator **Dina Lansey, M.S.N., R.N.**, Assistant Director for Diversity and Inclusion, focuses on increasing the participation of women and minorities in cancer clinical trials, establishing:

- Mandatory cultural competency training for all clinical faculty and staff members.
- Ongoing study prescreening, matching patients to available clinical trials.
- A new database with required participation by all clinical trial teams to track reasons patients decline clinical trials.
- Clinical trials education video series at hopkinsclinicaltrials.org
- Clinical trials brochure and decision tool (in process and currently being reviewed by the Johns Hopkins Kimmel Cancer Center Community Advisory Group).
- Transportation pilot study to remove the cost and availability of transportation as a barrier to participating in a clinical trial by providing free parking or transportation to Baltimore City residents participating in cancer clinical trials.

Smoking Cessation: Smoking remains the most preventable cause of cancer. **James Zabora, Sc.D.**, received CRF support to begin a pilot smoking cessation research effort to help members of families living in Latrobe Homes, a public housing development in East Baltimore that is home to 20,000 residents, quit smoking.

Community Advisory Groups: Community partners offer critical input and perspective to guide our experts as they plan for and provide community-based participatory education and research among minority and underserved populations in Maryland.

Day at the Market: This award-winning program is held twice a month at Northeast Market in East Baltimore to bring nurses, other clinicians, safety experts and others to offer tips on cancer prevention, screening, detection, treatment and healthy living.

Impact Through EMPaCT: Johns Hopkins is one of five universities selected to participate in Enhancing Minority Participation in Clinical Trials (EMPaCT), funded by the National Institute on Minority Health and Health Disparities. Jennifer Wenzel, Ph.D., is collaborating with diversity and inclusion expert Dina Lansey, M.S.N., R.N., and a patient navigator to improve cancer experiences for minority patients and care partners, and address existing disparities in health outcomes.

Cancer Alliance: The Merck Foundation provided a \$2 million grant to establish the Johns Hopkins Cancer Care Alliance. It represents a partnership among the Johns Hopkins Kimmel Cancer Center, Johns Hopkins Center to Reduce Cancer Disparities and the Johns Hopkins Clinical Research Network to improve health outcomes and to reduce and eliminate racial and ethnic health disparities.

Meet Our CRF Advisory Board

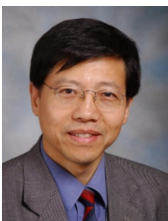
External advisory board members are acclaimed cancer researchers and leaders in cancer prevention and control from outside institutions. They review our progress reports and provide expertise to help guide the direction of our CRF-supported research.



Otis Brawley, M.S., M.A.C.P., is Chief Medical and Scientific Officer and Executive Vice President for Research at the American Cancer Society. He is a global leader in cancer prevention and control, promoting the goals of cancer prevention, early detection, and quality treatment through cancer research and education.



Mary Garza, Ph.D., M.P.H., is an expert in behavioral and community health at the University of Maryland School of Public Health and associate director of the Maryland Center for Health Equity. Dr. Garza worked as a health coordinator for a health center in Coachella Valley, California, where she gained valuable community-level experience working with low-income migrant farm workers, primarily Latinos and African-Americans.



Qingy Wei, M.D., Ph.D., is associate director for Cancer Control and Population Sciences at Duke University School of Medicine. He is an internationally recognized epidemiologist focused on the molecular and genetic epidemiology of head and neck cancers, lung cancer, and melanoma.



Honoring Anthony Alberg: Nationally recognized cancer researcher Anthony Alberg, Ph.D., M.P.H., was among the CRF External Advisory Board's founding members. He recently stepped down after being named chair of the University of South Carolina Arnold School of Public Health's Department of Epidemiology and Biostatistics.

Information Warehouse: Johns Hopkins CRF on YouTube

See discussions from our CRF-supported LunchLearnLink series. Topics include smoking cessation, cancer prevention, e-cigarettes, cancer disparities and much more. Visit <http://bit.ly/2nmo9U5> to watch.

CRF in Action

FY18 Awards
(January 10, 2017)
\$1,942,219

Grants:	All	New	FY Target
Translational Research	21	12	20
Faculty Recruitment	3	1	6
Faculty Retention	7	5	3
TOTAL	30	18	29

Steven An, Ph.D.: *Re-engineering the sensory array of prostate to discover novel chemo-mechanical signaling node against cancer metastasis.* **NEW**

Robert Anders, M.D., Ph.D., and Mark Yarchoan, M.D.: *Effect of transcatheter arterial chemoembolization and systemic therapy on the immune microenvironment in Hepatocellular Carcinoma.* **NEW**

Mary Armanios, M.D.: *Differential susceptibility of the female lung to genotoxic damage and to cigarette smoke.* **NEW**

Alexander Baras, M.D., Ph.D.: *Leveraging clinical somatic mutation profiling of malignancies with modern electronic health records to better characterize etiologic, prognostic, and therapeutic associations.* **CONTINUED**

William Bishai, M.D., Ph.D. and Trinity Bivalacqua, M.D., Ph.D.: *A potent rBCG as a therapeutic intervention for non-muscle invasive bladder cancer.* **NEW**

Kathleen Burns, M.D., Ph.D.: *Characterizing sequences and functions of LINE-1 endogenous mutagens.* **NEW**

Robert Casero, Ph.D.: *Role of spermine oxidase-generated H₂O₂, DNA damage and epigenetic changes in inflammation/infection-associated carcinogenesis.* **CONTINUED**

Geetanjali Chander, M.D., M.P.H., and Heidi Hutton, Ph.D.: *Development, cultural adaptation and piloting of an avatar delivered smoking cessation intervention for low income smokers in Baltimore City.* **CONTINUED**

Young Bong Choi, Ph.D.: *Preclinical evaluation of new vFLIP inhibitors to control HHV-8/KSHV.* **NEW**

Josephine Feliciano, M.D.: *A pilot study to assess an educational intervention to address distress and quality of life related to financial burden in advanced lung cancer patients.* **CONTINUED** *Pharmacy-Driven Smoking Cessation Pilot Program within a Multidisciplinary Cancer Clinic for Thoracic Malignancies.* **CONTINUED**

Jonathan Golub, Ph.D., M.P.H.: *COach2Quit: A novel mHealth smoking cessation application for cancer patients.* **CONTINUED**

Ahmed Hassoon, M.D., M.P.H., P.M.P.: *Novel Individualized Technology Intervention for Behavioral Change Among Cancer Survivors Among a High Risk Group: Artificial Intelligent Solutions to Increase Physical Activity.* **CONTINUED**

Christine Hann, M.D., Ph.D.: *Optimizing Bcl-2 inhibitor therapy for small cell lung cancer.* **CONTINUED**

Dina Lansey, M.S.N., E.N., O.C.N.: *Identifying barriers to therapeutic clinical trial participation using clinical trial candidate data.* **NEW**

Dina Lansey, M.S.N., E.N., O.C.N. and Ahmed Hassoon, M.D., M.P.H., P.M.P.: *Individual characteristics and research decisions in cancer care at Johns Hopkins.* **CONTINUED**

Kimberly Levinson, M.D., Ph.D.: *A novel screening strategy for adenocarcinoma of the cervix: The cervical cancer subtype on the rise in younger white women and older black women.* **NEW**

Noel Mueller, Ph.D., M.D.: *Examining gut micro-biota-mediated pathways in cancer etiology: A randomized controlled trial of metformin and weight loss in a biracial cohort of cancer survivors.* **NEW**

Elizabeth Platz, Sc.D., M.P.H.: *Estimating prevalences of liver fibrosis in those with and without risk factors for non-alcoholic fatty liver disease, a contributor to the rapid rise in liver cancer in Maryland: Phase 1 – Preparation.* **NEW**

Craig Pollack, M.D., M.H.S.: *Implementing an individualized risk prediction tool for men with prostate cancer: testing its impact on men with newly diagnosed cancer and expanding its capacity to men outside of Hopkins.* **NEW**

Richard Rodin, Ph.D.: *Developing a point-of-care test for human papilloma (HPV) vaccination status.* **NEW**

Ana Rule, Ph.D.: *Electronic Cigarettes as a Pathway of Exposure to Toxic and Carcinogenic Metals.* **CONTINUED**

Anju Singh, Ph.D. and Stephane Lajoie, Ph.D.: *Baltimore ambient particulate matter reprograms the immune system to facilitate tumor escape and progression.* **CONTINUED**

Katherine Smith, Ph.D.: *Implementing an individualized risk prediction tool for men with prostate cancer: testing its impact on men with newly diagnosed cancer and expanding its capacity to men outside of Hopkins.* **NEW**

Claire Snyder, Ph.D.: *Improving patient care and population health using patient-reported outcomes: developing a PRO core strategy.* **NEW**

Cristian Tomasetti, Ph.D.: *Mechanistic Model of Absolute Risk in Cancer.* **NEW**

Akila Viswanathan, M.D., M.P.H.: *Cervical cancer disparities in the DC and Baltimore Region and uncovering genomic differences by race.* **NEW**

Jessica Yeh, Ph.D. and Lawrence Appel, M.D.: *Metformin Treatment or Lifestyle Intervention to Improve Health in Overweight/Obese Cancer Survivors.* **CONTINUED**

Jessica Yeh, Ph.D. and Lawrence Appel, M.D.: *Establishing the Community-based Participant Engagement and Translation (CPET) Core: A developing core to facilitate intervention studies.* **NEW**

James Zabora, Sc.D.: *The East Baltimore Household-Based Smoking Cessation Program.* **CONTINUED**

A new oncology faculty recruit. **NEW**