

Johns Hopkins
CONQUEST

AN UPDATE FROM THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER ON
ITS MARYLAND CIGARETTE RESTITUTION FUNDS
2011

A Note from the Director

This is truly an exciting time to be a part of cancer medicine, and Maryland is on the forefront. Scientific breakthroughs by our investigators have revealed the unique genetic profiles for 88 types of cancer, including colon, breast, pancreatic, and brain cancers. This research, funded in part by the Maryland Cigarette Restitution Fund, has allowed us to begin altering the course of cancer in ways we could only imagine a few decades ago.

For the first time, we can begin to provide patients personalized therapies that target the unique cellular mistakes that initiate and drive their individual cancers. This new approach not only improves treatment outcomes but will also allow us to prevent many people from ever developing a cancer. It gives us the ability to accurately predict what drugs will work on which patients, and can tell us who needs regular cancer screening, and most importantly, who can be spared. The research supported by CRF improves care and has the potential to dramatically slash health care costs.

With this in mind, we cannot imagine a more appropriate partner in this work than the state of Maryland. As you can see, CRF programs have not only contributed to the health of Maryland citizens but also to the health of the state economy. We appreciate the continued commitment by our Governor and State lawmakers in the face of such difficult economic times. Every CRF dollar we receive is put to good use making cancer detection and treatment more effective and more efficient. CRF grants are critical to helping launch the research projects of bright, young faculty, who are then able to parlay this work into millions more in grants from other sources. We look forward to returning to full funding of the CRF research grant because while there is much we have accomplished together, we realize that until every patient is cured, there is still work left to do.



William G. Nelson, M.D., Ph.D.

Marion I. Knott Professor and Director

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

CRF FAST FACTS

- For every CRF research dollar spent, \$10 more is made through business contracts and other economic development.
- In 2010, Kimmel Cancer Center investigators earned one of the largest science and medicine grants under the American Recovery and Reinvestment Act, bringing millions in stimulus dollars to the State.
- Over a dozen CRF-based research discoveries and technologies have been patented or licensed to outside companies.

CRF: Improving the Health of Marylanders

Maryland Cancer Rates Continue to Decline

In the 1980s, Maryland ranked among the highest in cancer incidence and death rates. With targeted state initiatives, including the Maryland State Council on Cancer Control and the Cigarette Restitution Fund, these rates have steadily declined.

Maryland's Cancer Deaths

YEAR	Rankings
1983-1987	1 st
1999-2001	14 th
2005-2006	19 th
2007*	23 rd

**This is the most recent data available for all states.*

TRANSLATIONAL RESEARCH

A CRF Model for Cancer Discovery



RESEARCH: CRF investigator **Victor Velculescu, M.D., Ph.D.**, and team deciphered the unique genetic blueprint for colon cancer, revealing unique cellular alterations and the gene pathways through which they work.

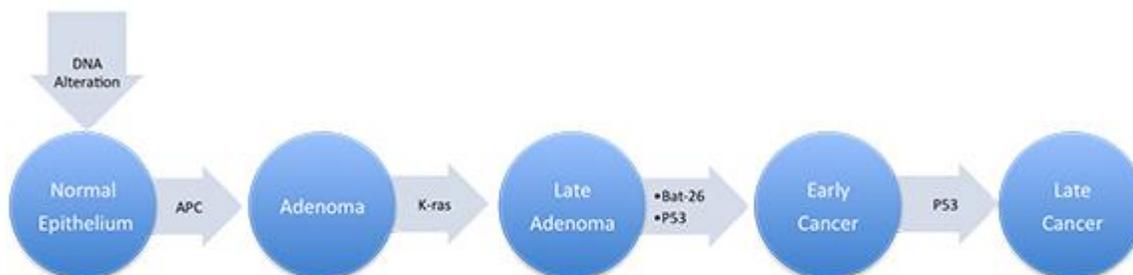
TRANSLATION: Velculescu and CRF investigator Luis Diaz, M.D., developed a simple, inexpensive blood test that can detect colon cancer DNA in circulating blood. The test could be used for early detection of colon cancer and to monitor for cancer progression and recurrence.

APPLICATION: The blood test is currently being studied in colon cancer patients to verify its accuracy.

POPULATION: Through a 2011 CRF research grant, **John Groopman, Ph.D., and Elizabeth Platz, Sc.D., M.P.H.**, are applying the blood test developed by Velculescu and Diaz to colon cancer screening.

Colon cancer is curable almost all of the time if it is detected early. Colonoscopy is currently the most effective way of detecting colon cancer and removing polyps in the colon that may cause colon cancer, but it has shortcomings. Colonoscopy cannot distinguish between benign polyps and precancerous ones. It is an invasive test with some associated risks and inconveniences, and, as a result, many people do not take advantage of it. Fewer than 70 percent of Marylanders comply with colonoscopy screening recommendations.

Groopman and Platz are studying the colon cancer blood test in patients for its ability to detect KRAS mutations in the circulating blood of people with adenomatous or precancerous polyps. This mutation is associated with dangerous polyps or adenomas that are genetically destined to become colon cancer. **If their studies confirm that the test can accurately pinpoint which polyps will become cancers, it provides a new simple, inexpensive, and virtually risk-free tool for colon cancer screening.**



CRF INVESTIGATOR: Shyam Biswal, Ph.D.

A Timeline of CRF Discovery



- **2001:** A cigarette exposure facility is constructed to study smoking-induced lung cancer.
- **2002:** The work reveals new information about smoking-related carcinogens and the cellular changes they cause that ultimately lead to lung cancer.
- **2003:** Biswal and team identify and test chemopreventive agents that block the negative impact of smoke on cells.
- **2004:** He identifies the Nrf2 gene and finds that it helps detoxifies cells of carcinogens, such as cigarette smoke. Nrf2 directs proteins to absorb pollutants and chemicals and then pumps them out, clearing cell of toxins.
- **2005-2007:** Another gene, called Keap1, is found to work with Nrf2. Keap1 lets cells know when toxins are removed, shutting down Nrf2.

The team learns that lung cancer cells corrupt the Nrf2/KEAP1 process. Biswal finds that an altered Keap1 gene keeps Nrf2 active pumping out cancer-attacking drugs before they can get into lung cancer cells.

Biswal used these findings to leverage additional grants from the National Institutes of Health and the Flight Attendant Medical Research Institute.

JHU reports three discoveries. Two international patent applications are based on this work.

- **2008-2010:** Biswal collaborates with a University of Maryland investigator to screen 1280 compounds for their ability to block Nrf2 in lung cancers with Keap1 mutations. The best candidate becomes the focus of clinical trials funded by the National Cancer Institute.

TODAY: This novel therapeutic approach to target lung cancer treatment resistance has resulted in three inventions licensed to the Baltimore, Maryland-based start-up company Cureveda. Patents are pending in the U.S., Canada, Europe, and Australia. **It is unlikely that this progress would have been made without the initial CRF grant.**

FACULTY SUPPORT

CRF Ignites Research Careers

CRF support plays an important role in the early research of young cancer investigators. Providing them seed funding early in their careers, these scientists are able to establish a body of research and successfully compete for additional public and private funding. Former CRF grant recipients, including Victor Velculescu, James Herman, Shyam Biswal, and Elizabeth Platz have become leaders in the fields of cancer genetics, epigenetics, and cancer prevention and control.

2011 Recipients:



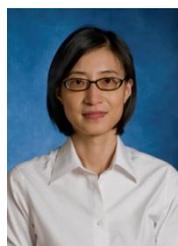
James Yager, Ph.D., received CRF support in 2009 to develop an animal model that resembles human breast cancer. With continued funding in 2011, he is studying how estrogen metabolism can alter gene expression and lead to breast cancer.



Christine Chung, M.D., is using molecular genetic information to develop targeted therapies for head and neck cancer.



Hans Hammers, M.D., Ph.D., is deciphering the mechanisms of antiangiogenesis treatment-resistance. These therapies work by cutting off the blood supply to tumors, and he is developing novel treatments for prostate and kidney cancers.



Hao Wang, Ph.D., is making much-needed advances in biostatistics, managing unusual data types related to cancer research to guide clinical investigators with clinical trial and biomarker development and population-based research.

CANCER SCREENING

Maryland is among the best in the U.S. in cancer screening, according to the Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance Survey. Though the Kimmel Cancer Center no longer receives CRF support for cancer screening in uninsured and minority populations, it remains a key initiative for our Center. Johns Hopkins Priority Partners, a Medicaid MCO with more than 185,000 participants, and Johns Hopkins community physicians, who care for more than 260,000 patients, continue to meet the needs of Maryland's underserved populations by providing screenings for colon, prostate, breast, and cervical cancers. Faculty from our gastrointestinal program have collaborated with representatives from the Baltimore City Health Department through its CRF Public Health Grant and provided colonoscopy screening to 200 uninsured Baltimore residents (FY11).

Building upon the community partnerships formed through the CRF, the Community Networks Program and the Center to Reduce Cancer Disparities were established. These programs, as well as a long-standing partnership with Howard University, are focused on developing research-based strategies to eliminate racial disparities in cancer death rates in Maryland and Washington, D.C.

LOOKING AHEAD

What We Can Accomplish with Full Funding

We appreciate the state's commitment to the CRF during these difficult economic times, and we look forward to full funding in 2013 and the opportunity to pursue these research endeavors:

- Research new technologies and clinical care strategies
- Study existing drugs for use in cancer prevention, and expand the use of promising therapeutic or diagnostic tools
- Expand cancer prevention science technologies and tools
- Recruit cancer epidemiologists with expertise in lung cancer and smoking, molecular epidemiology, and health services research
- Develop a Maryland cohort for cancer prevention and control studies