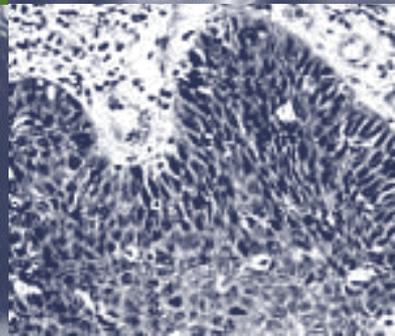




Cigarette Restitution Fund at Johns Hopkins

The Sidney Kimmel Comprehensive Cancer Center

John D. Groopman
Martin D. Abeloff



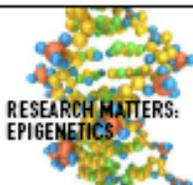
CONQUEST

A REPORT FROM THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER
ON ITS MARYLAND CIGARETTE RESTITUTION FUNDS

TAKING ON
MARYLAND'S
HIGH
PROSTATE
RATES



IN THE COMMUNITY



RESEARCH MATTERS:
EPIGENETICS



Cancer Prevention and Control

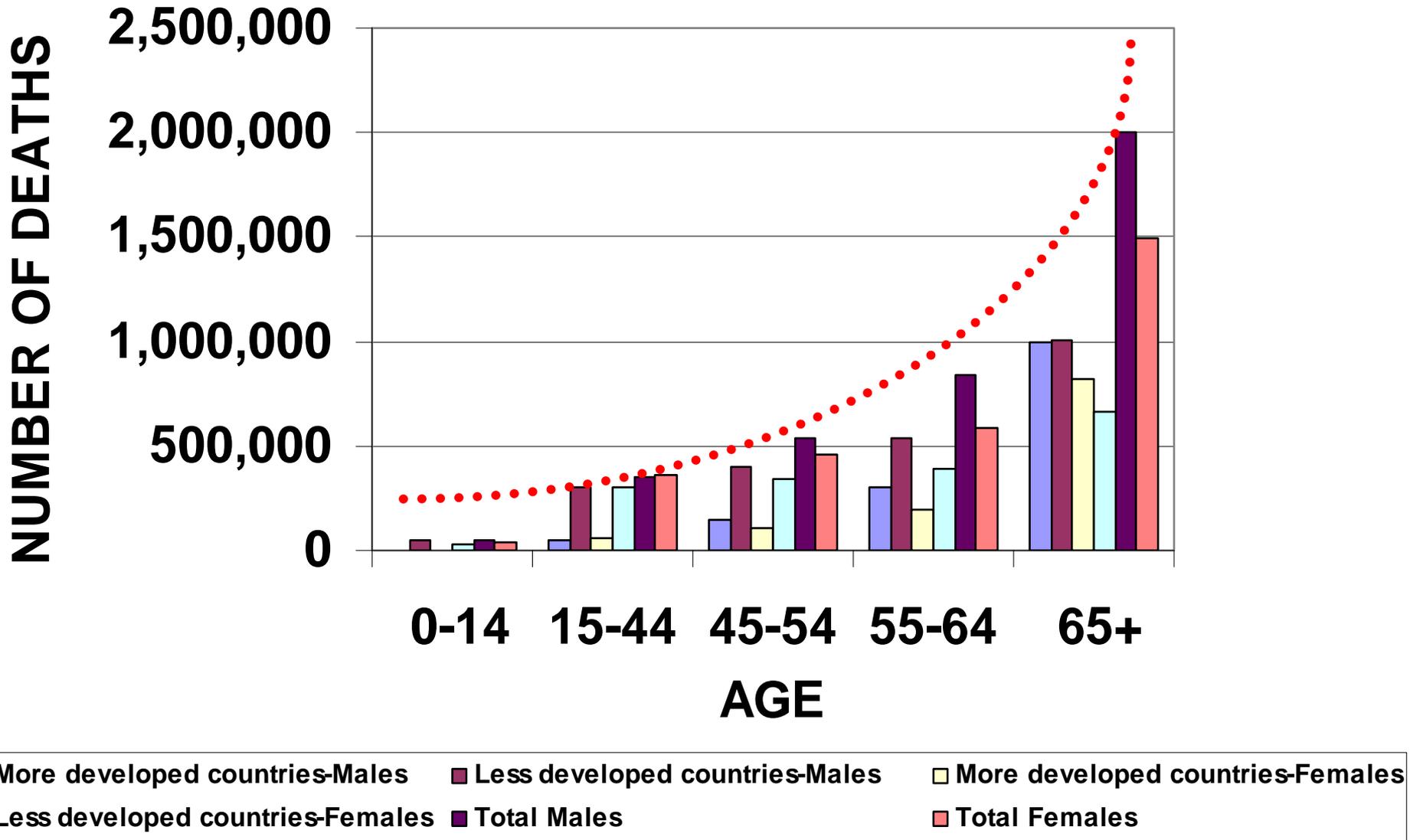
Working Towards a Cancer-Free Maryland

Hopkins Cancer Center Director
Martin D. Abeloff, M.D. dies of Leukemia

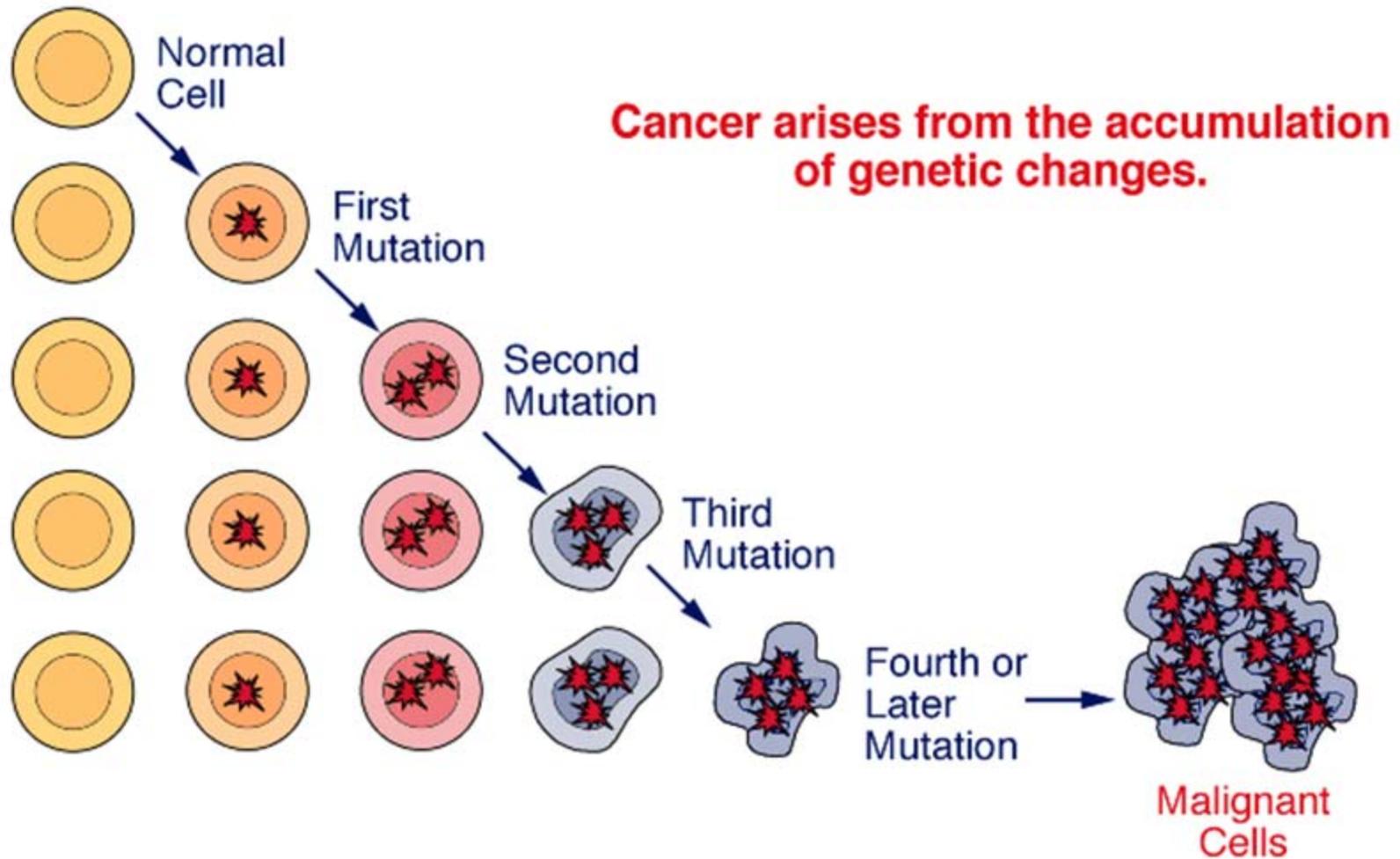


MARTIN D. ABELOFF
1942-2007

Cancer Mortality Worldwide



Understanding the Molecular Basis of Cancer



CRF Research Program Impact

**Prostate Cancer Demonstration Project and
Early Detection Initiatives:**

Viral Infection Epidemiology and Vaccines:

From populations to individual therapy

The Nrf2:Keap1 Pathway:

*Basic mechanisms translate into cancer
prevention*

CRF Research Program Impact

**Prostate Cancer Demonstration Project and
Early Detection Initiatives:**

Viral Infection Epidemiology and Vaccines:

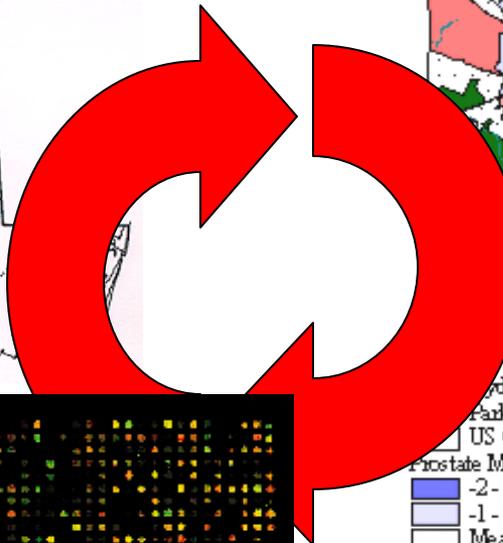
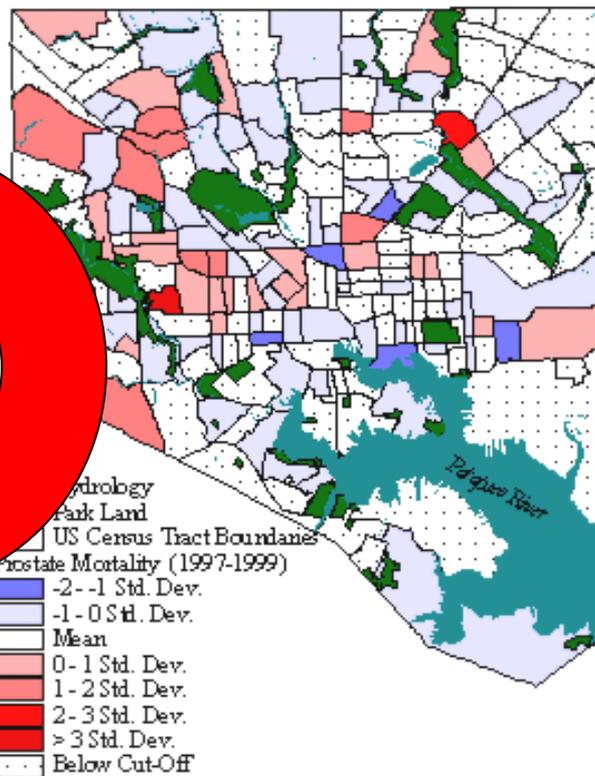
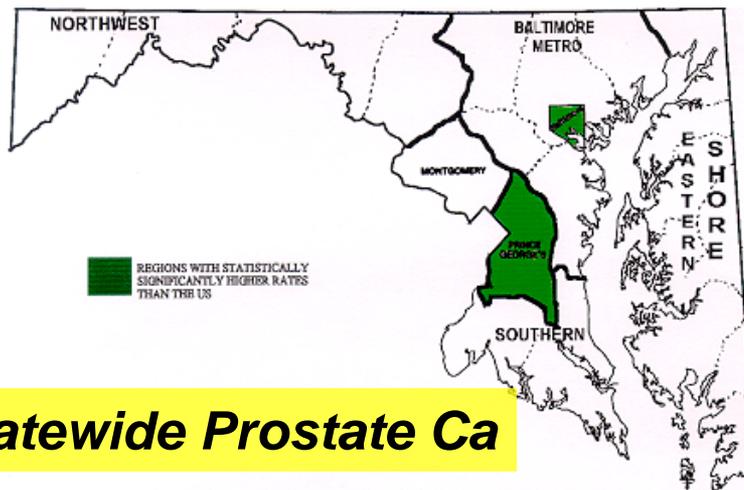
From populations to individual therapy

The Nrf2:Keap1 Pathway:

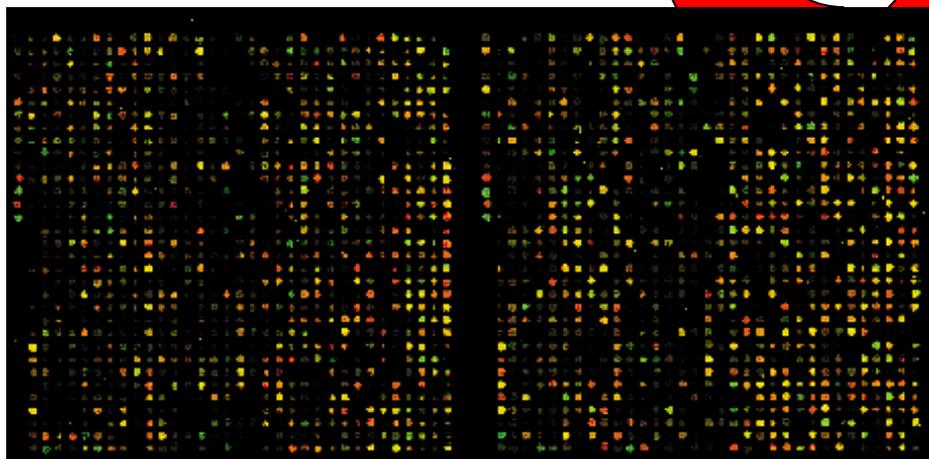
*Basic mechanisms translate into cancer
prevention*

Prostate Cancer Demonstration Project

Baltimore Prostate Ca

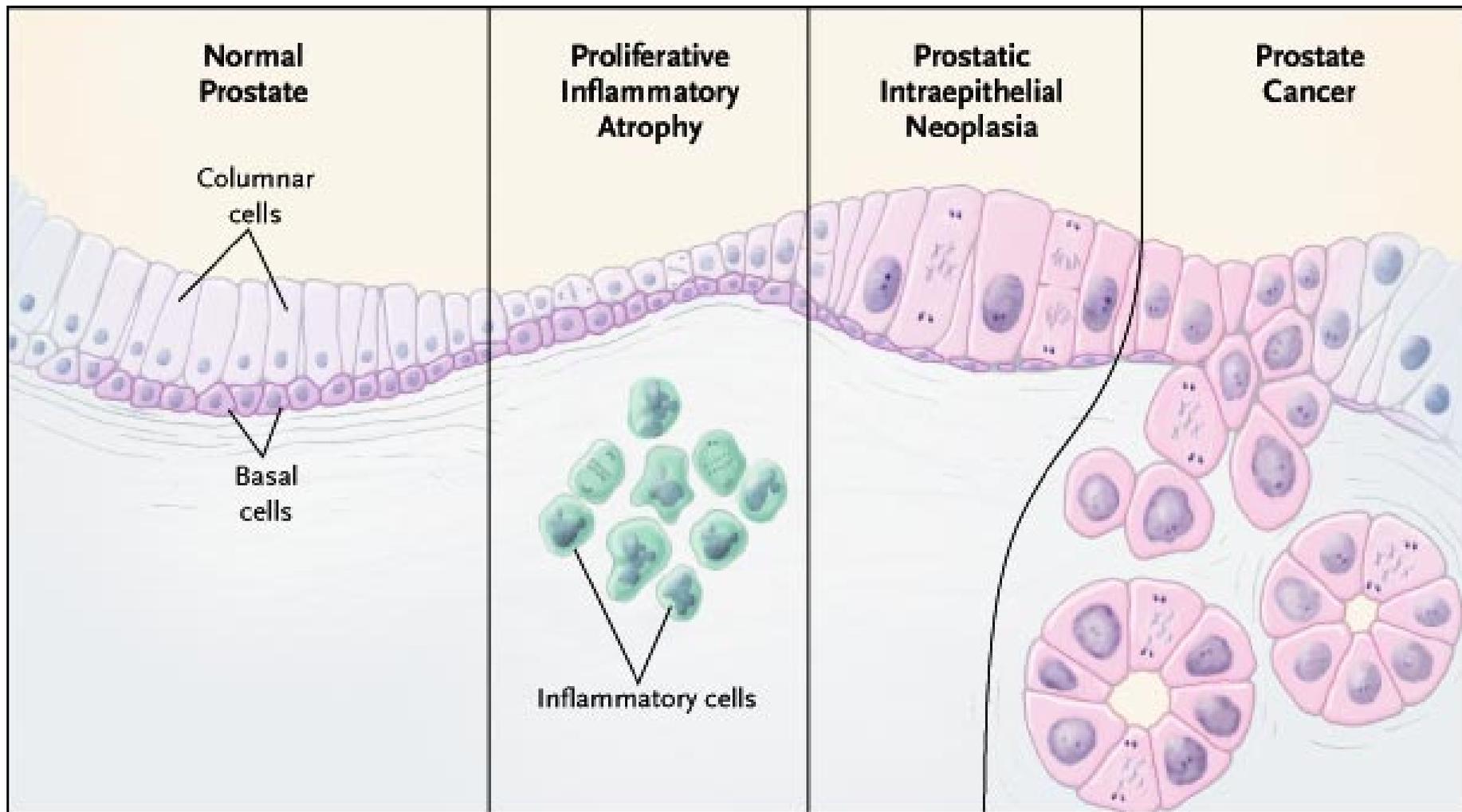


Statewide Prostate Ca



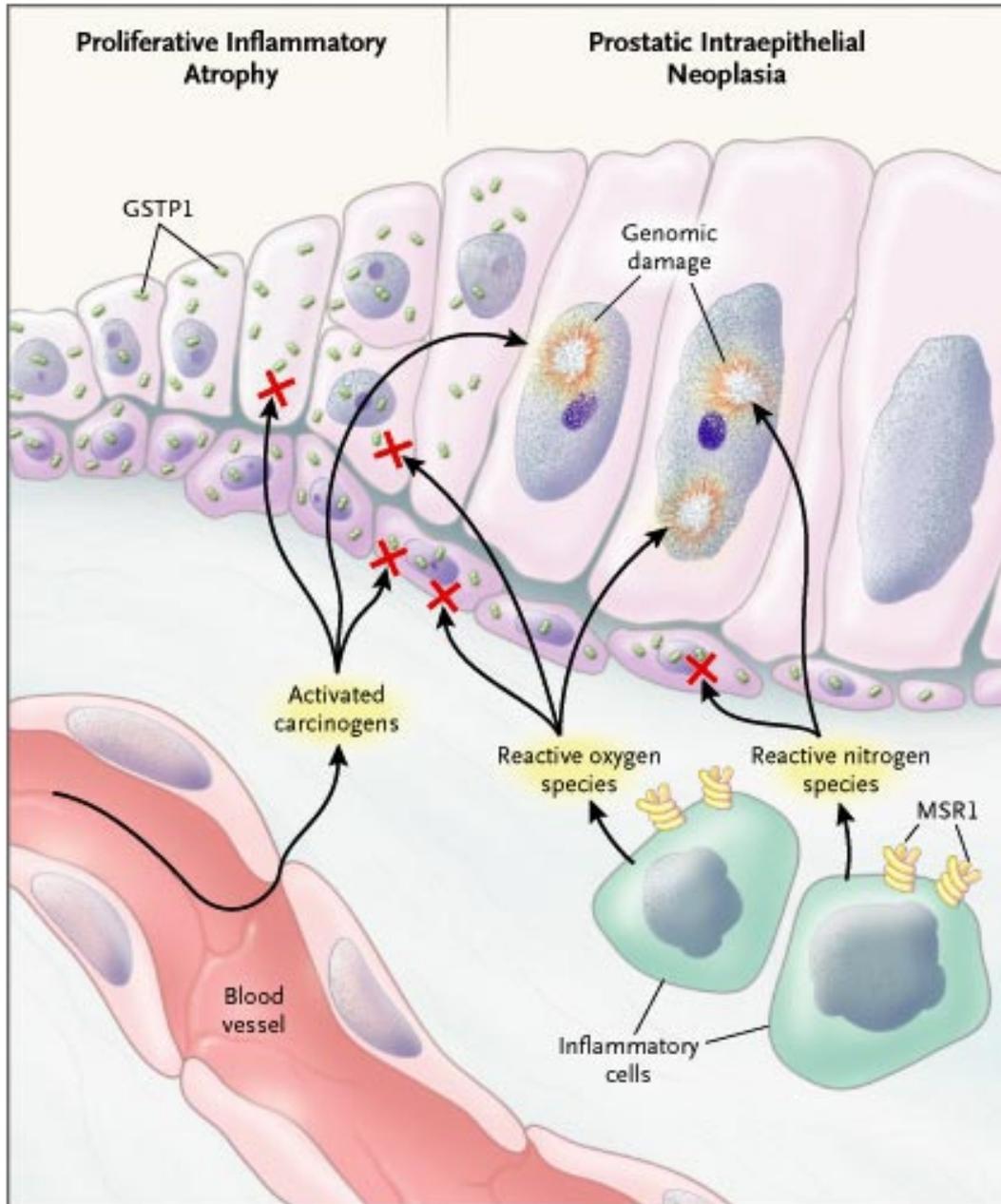
Mechanism(s) of Action

Proliferative Inflammatory Atrophy May be a Precursor to Prostate Cancer*



*Nelson WG *et al.* *New Engl J Med* 349: 366-81 (2003); Nakayama M *et al.* *Am J Pathol* 163: 923-33 (2003); Meeker AK *et al.* *Cancer Res* 62: 6405-9 (2002).

Inflammation as a Cause of Prostate Cancer*



*Nelson WG *et al.* New Engl J Med, 349: 366-81, 2003

CRF Seeds Scientific Advances and Leveraging

Faulty DNA repair gene linked to tobacco use is identified

Saliva test for HPV16 tested

DNA change predicts head and neck cancer

ADDITIONAL FUNDING

NIH-RO1 Award: \$200,000

Damon Runyon Award: \$970,000

FAMRI Award: \$108,000

Awarded 2000 Gene profile identifies tissue at high risk of cancer

INFRASTRUCTURE

State-of-the-art equipment and analyses for cancer-related DNA alterations

COLLABORATIONS

University of Maryland/JHU Project

SKCCC Head & Neck Cancer SPORE

Johns Hopkins School of Public Health

Surgical margins study



Joseph Califano III, MD

A 2000 CRF grant initiated research to improve cancer outcomes and detect oral cancer early through DNA profiling.

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Cervical Cancer

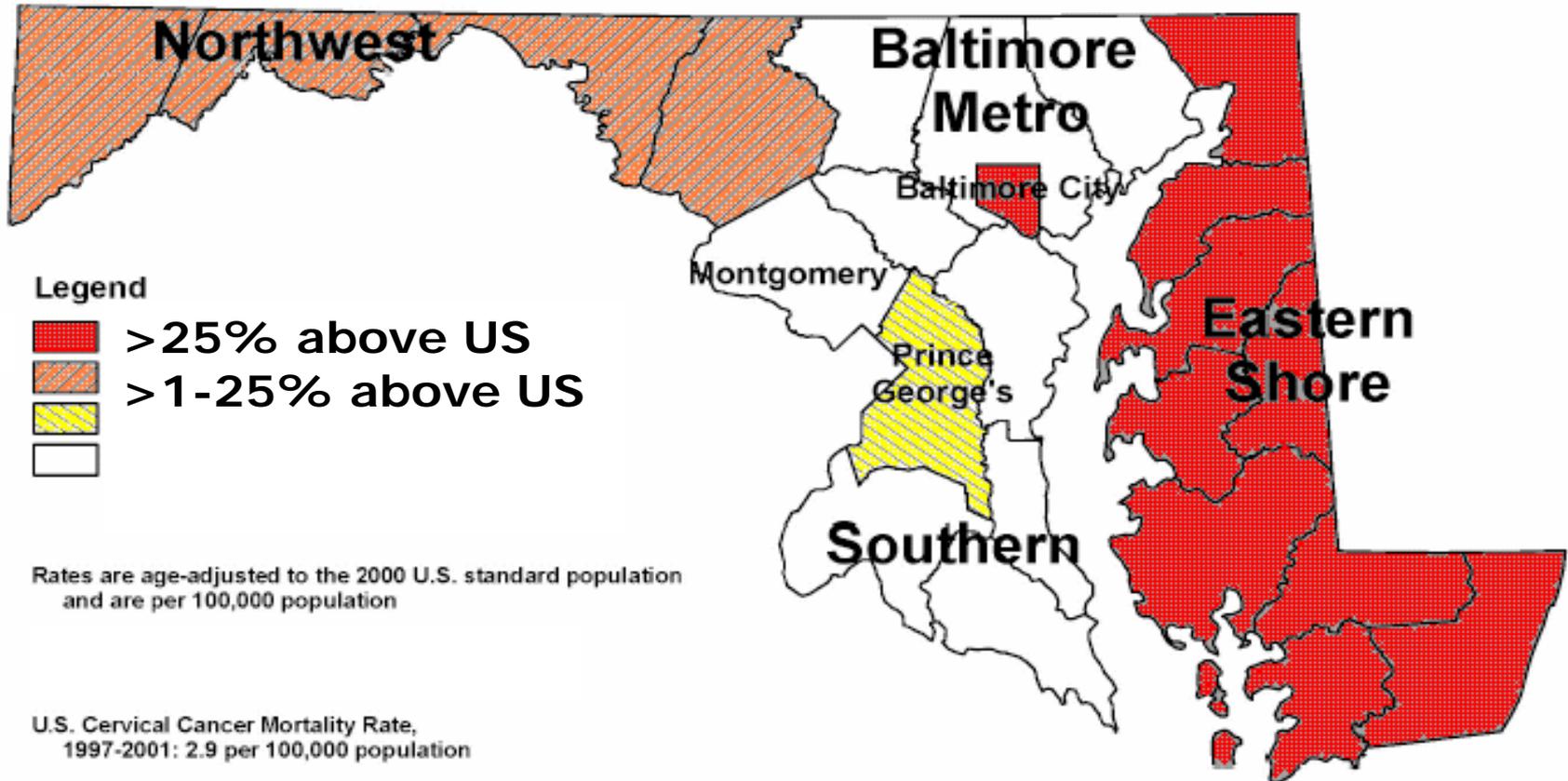
Prevalence: 2,274,000 women have cervical cancer¹
Incidence: 510,000 new cases each year¹

**2000 estimated incidence of invasive cervical cancer
by selected region²:**



Mortality: Second leading cause of female cancer-related deaths (288,000 annually)¹

Epidemiology of Viral Infections and Vaccine Interventions: From Mapping to Translational Research: Maryland Cervical Cancer Mortality (1997-2001)



Source: Maryland Division of Health Statistics, 1997-2001

CRF Investigators and Cervical Cancer Prevention



Trimble **awarded CRF grants** to investigate HPV vaccine and establish Cervical Diseases Center.

2001

Established Cervical Diseases Center in East Baltimore to offer **outreach and coordinated care for women** with HPV disease.

2002-2003

Began investigating ways to stimulate an immune reaction against cells infected with HPV and prevent the progression to cervical cancer.

Leveraged CRF-funded research into a **five year grant of \$700,000** from the National Cancer Institute.

2003-2008

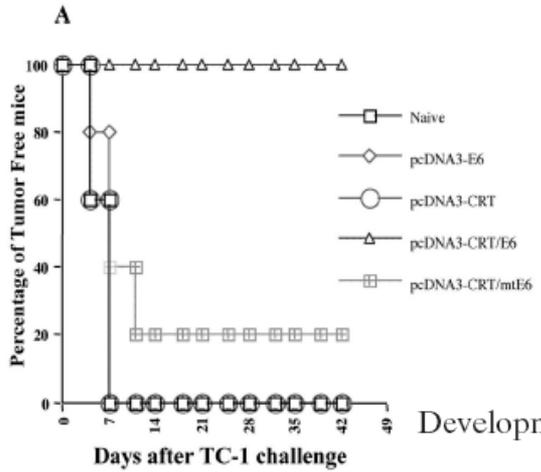


Launched Phase I clinical trials of a unique therapeutic **cervical cancer vaccine**, aimed at curing established disease. It is a landmark study because **1/3 of participants are minority women**—more than double the National average.

2004

Negotiating with a private industry partner for **licensing and distribution** of vaccine

2005



Development of a DNA Vaccine Targeting Human Papillomavirus Type 16 Oncoprotein E6

JOURNAL OF VIROLOGY, Aug. 2004, p. 8468-8476

2007



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**MARKET STAGE
BROCCOLI**



150 grams

3-DAY SPROUTS



3 grams

**FREEZE-DRIED
SPROUT EXTRACT**



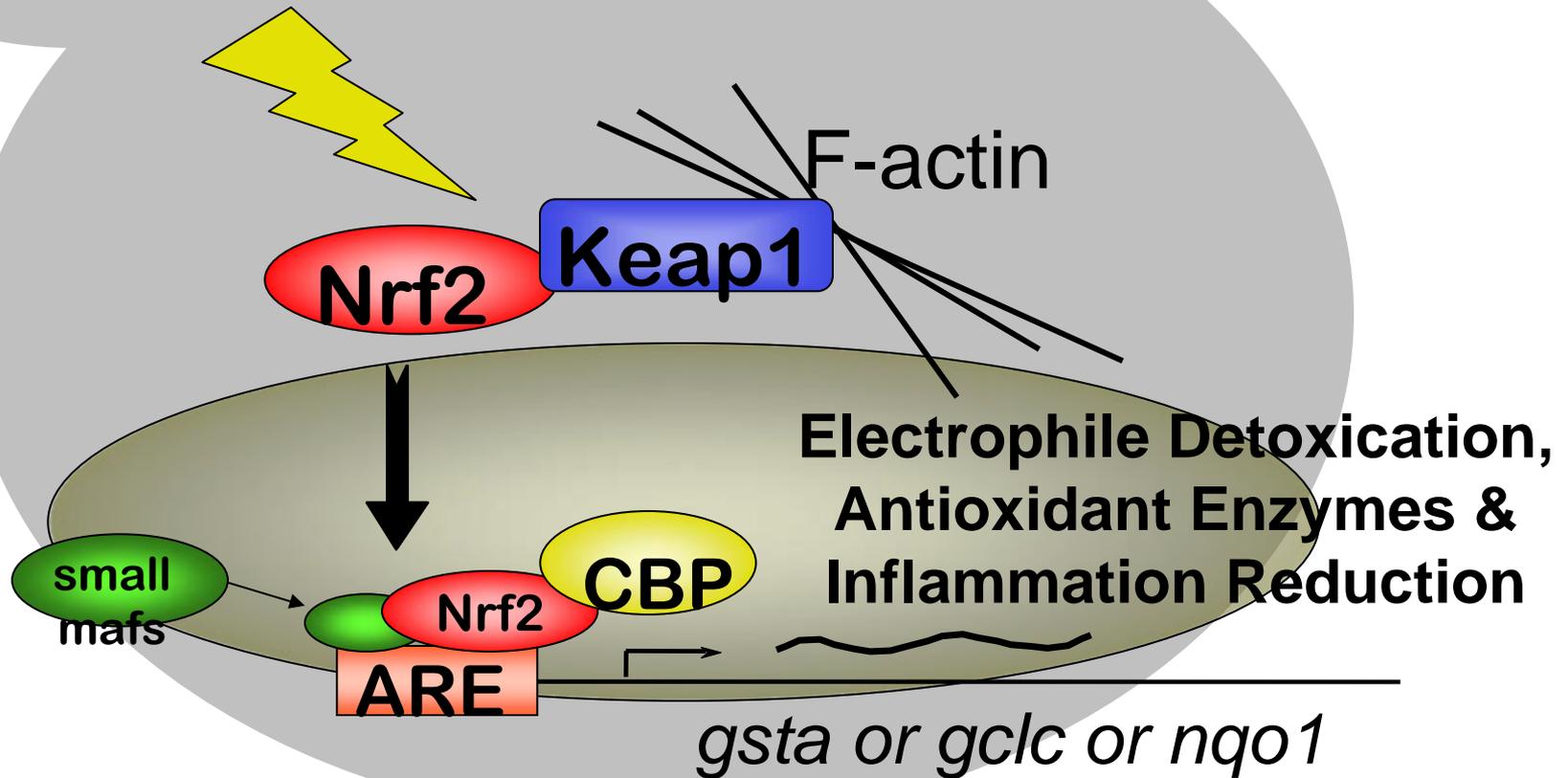
150 mg

**All preparations contain the same quantity
of detoxication enzyme inducer activity**

Basic Mechanisms in the Nrf2:Keap1 Pathway to Cancer Prevention

Enzyme Inducer
(dithiolethiones,
isothiocyanates
triterpenoids)

J. Clin. Inv 114:1248-59, 2004
PNAS 101:2040-5, 2004
JBC 278:8135-45, 2003
Cancer Res 62:5196-203, 2002



Nrf2: Molecular Target to Intervention Trials at SKCCC

Identification of Inducers

- dithiolethiones
- isothiocyanates (sulforaphane/broccoli)
- triterpenoids

Genetic Models: Nrf2 Knockout Mice

- increased sensitivity to;
- environ. carcinogens
 - smoke-induced emphysema
 - oxidative stress

Ongoing Phase I and II Clinical Interventions with Nrf2 Activators

- * healthy volunteers
- * men undergoing prostatectomies
- * women undergoing breast reduction surgery
- * heavy smokers/high risk for lung cancer
- * high risk for liver cancer

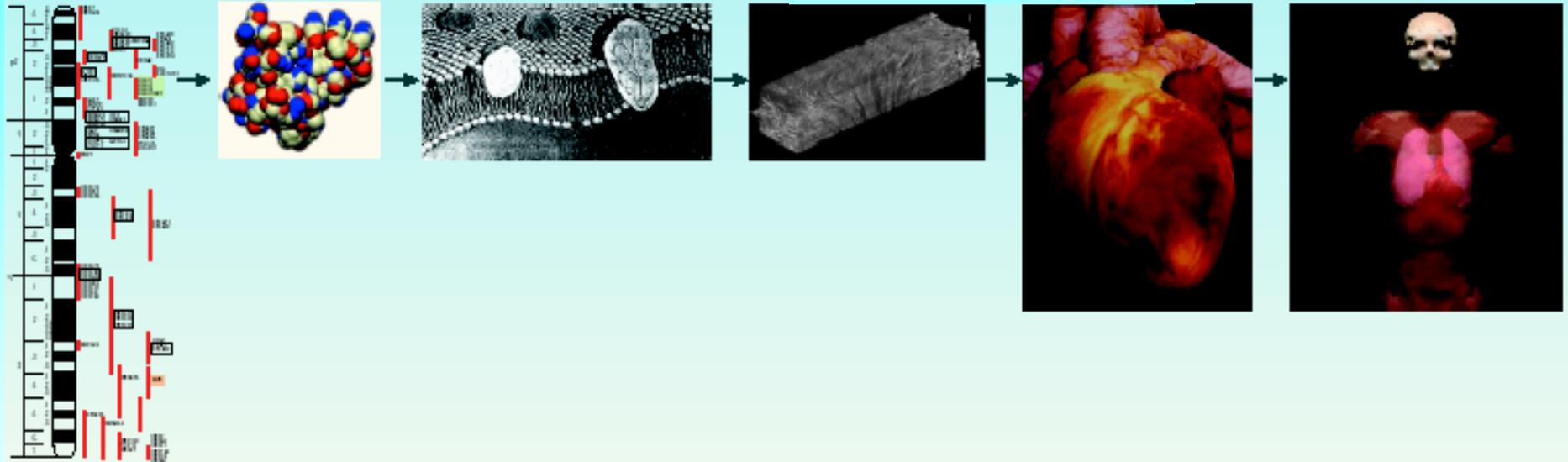
Biomarker Development and Validation

- gene expression markers
- genotoxicity markers

Pre-Clinical Efficacy *in vivo*

- pharmacology/toxicology
- chemoprevention models

Genes → **Proteins** → **Cell Structure & Function** → **Tissue Structure & Function** → **Organ Structure & Function** → **Clinical Medicine**



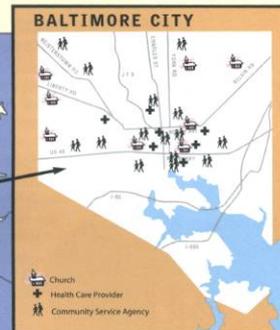
35,000+ genes → 100,000+ proteins → 300+ cell types → 4 tissue types → 10 organ systems → 1 body

Toxins and Toxicants **Biological Response**

The state of cancer in Maryland

- Oral cancer screening
- Faith-based cancer prevention and control
- Youth smoking cessation
- Lung cancer risk factors for women
- Biomarkers for colon cancer
- Racial/ethnic differences in prostate cancer
- Cancer prevention in African Americans
- Cervical cancer prevention in Hispanics
- Cadmium exposure and prostate cancer risk
- Genetics of lung cancer
- Urban disparity cancer reduction
- HPV infection and oral cancer
- Cervical cancer vaccine
- Environmental exposures to carcinogens
- Racial disparities and cervical cancer
- Waterway contamination and cancer risk
- Prostate, breast and colon cancer screening

CENTRAL MARYLAND (INCLUDES BALTIMORE CITY)



WESTERN MARYLAND:

- Smoking-related cancers
- Carcinogens in drinking water
- Cancer risk from arsenic exposure
- Youth smoking cessation

BEFORE AND AFTER

BEFORE CRF:

Maryland ranked fourth nationally in cancer deaths in 1990.

AFTER CRF:

Maryland now ranks 17th nationally in cancer deaths.

BEFORE CRF:

Maryland cancer mortality rates remained steady.

AFTER CRF:

Maryland's cancer mortality rates are dropping at twice the national average.

BEFORE CRF:

Overall cancer death rates were 27 percent higher among Maryland's minorities when compared to whites.

AFTER CRF:

In 2001, cancer death disparities between Maryland whites and minorities declined significantly. Cancer research is targeted specifically to reducing the cancer burden among the state's minority populations.

BEFORE CRF:

There was no central Core Population Resource for the collection and study of blood samples.

AFTER CRF:

A Core has been established and more than half of patients and their friends and family members have said they want to provide blood samples to help identify biomarkers for cancer prevention and control.

STATEWIDE

- Carcinogens in Maryland's air, water, and soil
- Smoking-related cancer detection and prevention
- Breast cancer gene pathways
- New cancer drug discoveries
- Analysis of genetic risk for colon cancer
- GIS survey of environmental risks for colon cancer
- Inflammation and cancer risk
- Core Resource for cancer biomarker discovery.
- Overcoming breast cancer treatment resistance
- Familial and early markers of pancreatic cancer.
- Cholesterol-lowering drugs for prostate cancer prevention.

WHEN MARYLAND INVESTS, OTHERS DO TOO.

Direct funding leveraged through CRF:

Sidney Kimmel:	\$150 million
FAMRI:	\$15 million
Dept. of Defense:	\$10 million
Avon Foundation:	\$1.5 million

* Flight Attendants Medical Research Institute

SOUTHERN MARYLAND (INCLUDES SUBURBAN D.C. AREA):

- Racial/ethnic variations in prostate cancer
- Cancer biomarkers and prevention
- Cancer risk from arsenic exposure

EASTERN SHORE:

- Carcinogens in drinking water
- Cancer risk from arsenic exposure
- Youth smoking cessation

CRF COMMUNITY OUTREACH

Through the CRF Public Health Grant, more than 1.9 MILLION citizens have been reached. More than 54,000 have met with a cancer educator to learn about cancer screening for early detection. Over 2,000 men have been screened for prostate cancer resulting in TEN diagnoses of cancer.

