



# Duke Prostate Center News

DUKE UNIVERSITY MEDICAL CENTER

## The DPC Joins the Department of Defense Prostate Cancer Consortium

**2**  
Prostate Cancer Nomogram

**3**  
Flaxseed Trial

PSA Velocity

**4**  
Genomic Predictors  
RNA Aptamer: Trojan Horse?

**5**  
Clinical Trial Corner

**6**  
DPC Members

On January 1, 2007, the Duke Prostate Center (DPC) became one of 10 academic medical centers nationwide selected to participate in a cooperative group dedicated to advancing new therapies and improving treatment outcomes in men with prostate cancer.

It is expected that this consortium will open the access to trials for patients in North Carolina and the surrounding region, provide additional support for the DPC's infrastructure, and provide resources to conduct larger scale multi-center trials initiated at Duke.

Several DOD trials are already under way at Duke, including novel agents given prior to radical prostatectomy, antiangiogenic therapy for advanced metastatic disease, and other novel agents for patients who are no longer responding to standard therapies.



In joining the DOD consortium, the Duke Prostate Center has positioned itself as a center of excellence in prostate cancer research, dedicated to innovative strategies to reduce the burden of illness caused by advanced prostate cancer.

For more information on this consortium, visit [cdmrp.army.mil/pcrp](http://cdmrp.army.mil/pcrp).

## The Obesity-Prostate Cancer Connection

In the past several decades, obesity has become a problem of epidemic proportions. Only recently have investigators begun studying the link between obesity and prostate cancer in earnest with DPC urologist, Stephen Freedland, MD, and his team taking a lead role.

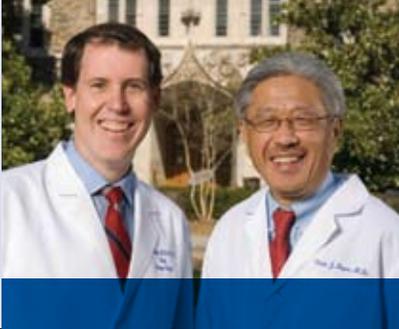
In a landmark study published in *JAMA*, Dr. Freedland and colleagues found obese men with prostate cancer have nearly 20 percent lower PSA levels than normal-weight individuals, possibly as a result of larger blood volume (dilution). If this is not taken into account when screening for prostate cancer, cancers may be missed in obese men.

Dr. Freedland's group has already established that obese men have larger prostates, thus

making biopsy harder to find cancers in obese men. Dr. Freedland's group was also the first to show that obesity is a risk factor for cancer recurrence after surgery, and he suspects that missing cancers and delayed diagnosis may in part help explain this observation.

Dr. Freedland is actively involved in understanding why obese men develop more aggressive cancer, with a special focus on the role of diet in prostate cancer. In the meantime, he suggests that interventions to get people to lose weight and to more aggressively screen patients with obesity for prostate cancer may be beneficial.

*JAMA* 2007, 298:2275-80.



Judd Moul, MD  
Chief, Division of Urologic Surgery  
Director, Duke Prostate Center

Judd Moul, MD, with Victor J. Dzau, MD, Duke University chancellor for health affairs and president and CEO of Duke University Health System.

## From the Editor

The Duke Prostate Center represents a multidisciplinary collaboration of physicians, scientists, and dedicated health care providers whose mission is to provide clinical and research-based care to patients with prostate cancer using a team approach. Through our new leadership, clinical space, and research agenda, we hope to improve the outcomes of men with prostate cancer, both locally and on the national level.

In this issue you will find highlights of our mission, our members, and our initiatives to bring quality to prostate cancer care.

## DPC Researchers Develop Model to Predict Outcome in Advanced Prostate Cancer

For men who have advanced prostate cancer, there are many treatment options, including chemotherapy, hormonal therapies, and clinical trials of novel agents. Estimating prognosis at this stage can be very challenging, however, given the many different situations that patients are faced with.

Now, DPC researchers, led by Andrew Armstrong, MD, have developed tools that allow for improved prognostic information that will allow physicians to communicate more effectively with patients.

Dr. Armstrong worked with researchers at Johns Hopkins University and other institutions to develop a nomogram, which is a predictive tool for men with hormone-refractory prostate cancer, based on a large study of over 1,006 men treated with various types of chemotherapy drugs. This study (TAX327) formed the basis for the approval of docetaxel (trade name Taxotere) and is the largest to date in this setting.

They identified 11 clinical variables that collectively predicted a man's one-, two-, and five-year survival. This model may be useful for future studies to help develop new drugs and allow the patient and physician to make

decisions about when to start aggressive therapy based on this prognosis.

By understanding the natural history of this disease, these researchers hope to identify new drugs that may improve this natural history. In addition, Dr. Armstrong and colleagues have identified changes in PSA and pain following the initiation of chemotherapy to have strong prognostic significance, allowing the physician and patient to individually tailor treatment over time.

These studies may help inform endpoints for clinical trials in advanced prostate cancer and provide useful information to patients over time during the course of therapy.

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J Clin Oncol 2007, 25:2965.

Clin Cancer Research 2007, 13:6396-6403.



The European yew tree, from which the drug Taxotere is derived.

## Flaxseed Appears Beneficial in Early Prostate Study

**F**laxseed is a rich source of plant lignans and omega-3 fatty acids, both of which may have cancer preventive properties through alterations in hormonal signaling and inflammation. Duke Prostate Center researchers piloted flaxseed in earlier studies, finding reductions in PSA and proliferation in prostate tissues.

Now, Duke has conducted a multi-center randomized trial of flaxseed, low-fat diet, the combination, or a usual diet in men with prostate cancer prior to surgery. In the trial, 161 men were randomized, and all treatment arms were well tolerated for approximately four weeks.

The primary endpoint—proliferation rate—was significantly reduced in the flaxseed arm (3.2% vs. 1.7%,  $p=0.0013$ ), indicating potentially true biologic activity for flaxseed. A low-fat diet had no effects other than a lowering of cholesterol. While PSA values did not differ across study arms, this trial confirms the biologic activity of flaxseed and opens the possibility of examining flaxseed in a larger prostate cancer prevention trial.

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Proceedings of the American Society of Clinical Oncology, 2007 abstract 1510.

## PSA Velocity Is a Useful Tool for Prostate Cancer Diagnosis

**I**n recent years, PSA screening has been much criticized for its lack of accuracy in predicting for the development of prostate cancer. Judd Moul, MD, and colleagues used the DPC database to look at this test from a different perspective, focusing on its rate of change over time—or velocity.

They found that PSA velocity can add to PSA testing in helping to decide which men may need a biopsy. Particularly in young men under the age of 60, a PSA velocity greater than 0.4ng/ml/year was found to be the most sensitive measure to detect prostate cancer, and did so while maintaining a reasonable false positive rate.

In addition, lowering the PSA threshold from 4.0ng/ml to 2.0ng/ml improved cancer detection rates in young men, but also at a cost of higher false positives. These results indicate that PSA screening may be improved through the use of PSA velocity and emphasize the need for more accurate ways to detect prostate cancer and avoid unnecessary biopsies.

This study also highlights the differences in PSA thresholds for biopsy in younger men who may have smaller prostates, and it has wide-ranging implications for men undergoing prostate cancer screening worldwide.

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J Urol 2007, 177:499-504.



## Genomic Profiling of Prostate Cancer: Personalized Medicine

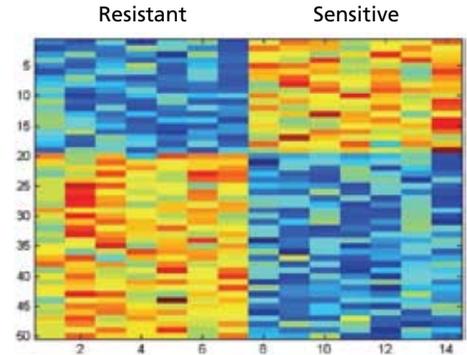
The ability to individually predict benefit from targeted agents, including chemotherapy, in prostate cancer is the hallmark of personalized medicine. Genomic medicine based on molecular signatures has revolutionized the way we look at cancer, and for the first time is allowing individually tailored medicine into the clinic.

Phillip Febbo, MD, and colleagues from the DPC and the Institute for Genome Sciences and Policy (IGSP) at Duke have developed genomic signatures to predict the response to chemotherapy in several cancers, including prostate cancer. By validating these tests in men with advanced prostate cancer, they hope to identify men prior to treatment who have the most to gain with chemotherapy and other therapies.

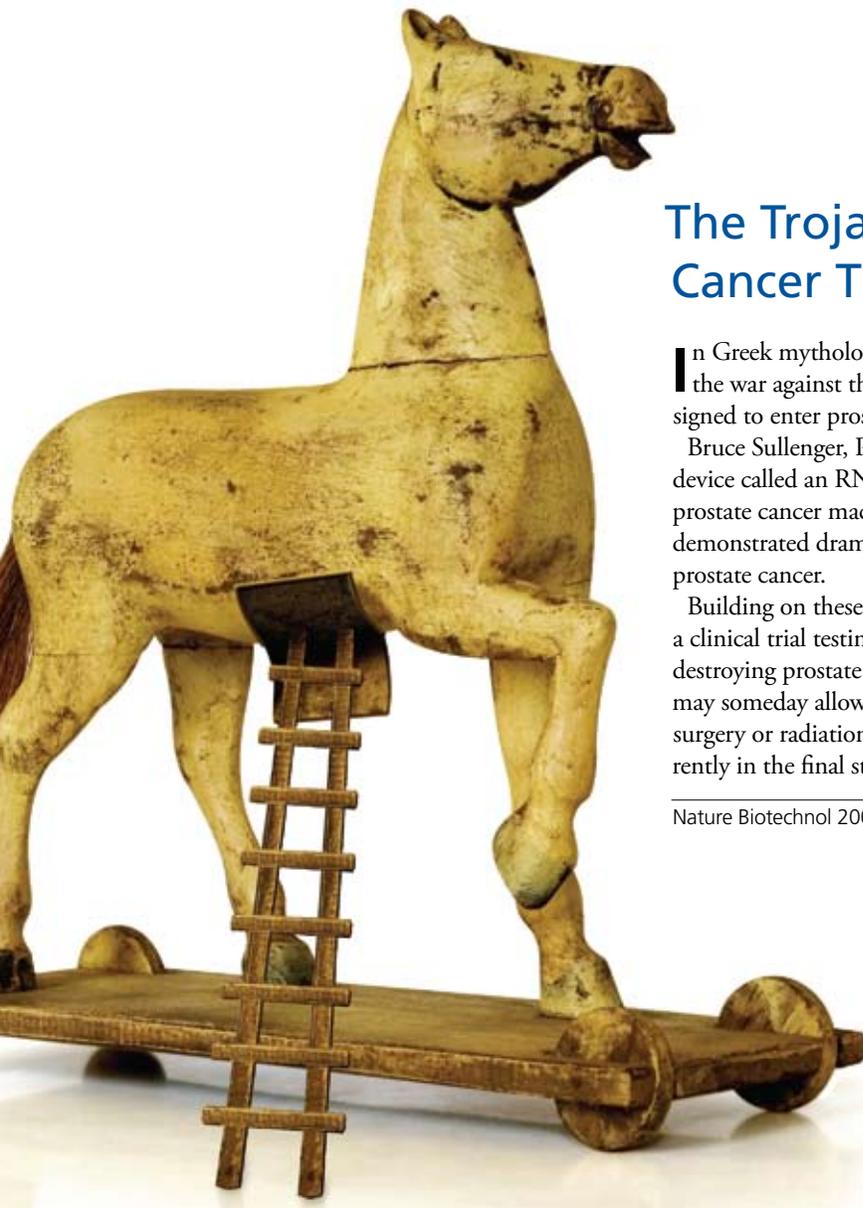
In addition, they can use these signatures to identify other potential ways of treating cancers that may not have been thought of before. By looking directly into the cancer cell machinery, they may be able to decipher the code that unlocks the complexity of this disease and opens the door to newer treatments. The goal is clearly to prolong life without suffering from this illness, using drugs that can be individually tailored to men who need them the most.

Drs. Febbo, Armstrong, and George are also developing a new class of compounds called mTOR inhibitors for men with prostate cancer. Using genomic medicine to identify markers of sensitivity and resistance to this therapy may one day lead to improved cocktails of treatments for this disease.

Nature Medicine 2006, 12:1294-1300.



Cancer cell gene expression profiles may unlock the complexity of prostate cancer and improve on current therapies.



## The Trojan Horse of Prostate Cancer Therapy: RNA Aptamers

In Greek mythology, the Trojan horse was used to enter the gates of Troy and win the war against the Trojans. In cancer research, a novel Trojan horse has been designed to enter prostate cancer cells and destroy them from the inside.

Bruce Sullenger, PhD, and colleagues developed a specialized molecular homing device called an RNA aptamer to target cancer cells and used a “smart bomb” against prostate cancer machinery to induce the cancer cells to stop growing and die. They demonstrated dramatic specificity and reduction in tumor size in mouse models of prostate cancer.

Building on these findings, Daniel George, MD, and colleagues have developed a clinical trial testing this new method in men with prostate cancer. By selectively destroying prostate cancer cells while sparing normal prostate tissue, this approach may someday allow men to receive therapy for prostate cancer without the need for surgery or radiation and the risks associated with these treatments. This study is currently in the final stages of development and projected to begin accrual in 2009.

Nature Biotechnol 2006, 24:1005-1015.

## LOCALIZED DISEASE

### Pre-operative Trials

1. **Radiation.** Drs. Koontz and Lee are investigating the use of lower doses of radiation to eliminate prostate cancer cells that may be outside of the prostate prior to undergoing radical prostatectomy.
2. **Novel agents.** Drs. George, Armstrong, and Febbo are investigating the use of several drugs intended to interfere with the normal growth of prostate cancer (sunitinib, rapamycin, bevacizumab, and chemotherapy) for men with high-risk prostate cancer prior to undergoing radical prostatectomy.

### Surgical Trials

1. **Cryotherapy.** Dr. Polascik is investigating the use of focal prostate cancer therapy (cryotherapy) to treat prostate cancer without removal of the entire prostate.

### Radiation Treatment

1. **Chemotherapy following radiation.** For men at high risk for recurrence after radiation and hormonal therapy, Duke is participating in a multi-center trial of chemotherapy given after completion of radiation.
2. **Lower doses of radiation.** Dr. Lee and colleagues are investigating the use of shorter but more intense time periods (5.5 weeks vs. 8 weeks) of radiation treatment for men with low-risk disease in this multi-center trial.

## ADVANCED DISEASE

### Prevention of Fractures

1. **Zoledronic acid.** Duke is participating in a multi-center trial of an intravenous medication to prevent or delay the risk of bone fractures in men with metastatic prostate cancer.

### Novel Agents

1. **Chemotherapy plus novel agents.** Drs. George, Armstrong, and Febbo are investigating the combination of promising novel agents with or without standard-of-care chemotherapy treatments for men with recurrent and/or metastatic prostate cancer. These treatments include inhibitors of tumor blood vessel growth, inhibitors of prostate cancer cell growth and function, and therapies that work on the immune system to destroy prostate cancer.
2. **mTOR inhibitors.** The DPC contains a multidisciplinary team of investigators who are looking at ways to prevent prostate cancer cells from spreading and growing, using a new class of medications called mTOR inhibitors. One of these agents was recently FDA-approved for kidney cancer treatment, and investigators at the DPC are researching the use of these medications for men with prostate cancer.

# FACULTY MEMBERS IN THE DPC

## UROLOGY (SURGERY)



Judd W. Moul, MD, FACS, Chief



Stephen J. Freedland, MD



Thomas Polascik, MD



David M. Albala, MD



Tracey L. Krupski, MD



Cary N. Robertson, MD



Greg D. Bianchi, MD

“Duke takes the team approach to prostate cancer, giving men state-of-the-art options in prevention, screening, treatment, and survivorship.”

—Andrew J. Armstrong, MD, ScM  
Editor, *Duke Prostate Center News*



Craig F. Donatucci, MD



Kelly E. Maloney, MD



Philip J. Walther, MD, PhD

## RADIATION ONCOLOGY



Carol Hahn, MD



Bridget Koontz, MD



W. Robert Lee, MD



Robert Prosnitz, MD



Zeljko Vujaskovic, MD, PhD

## MEDICAL ONCOLOGY



Andrew J. Armstrong, MD, ScM



Phillip G. Febbo, MD



Yuri Fesko, MD



Daniel J. George, MD



Veshana Ramiah, MD

## PATHOLOGY



Leslie G. Dodd, MD



John Madden, MD



Robin T. Vollmer, MD

# What is the Duke Prostate Center?

The DPC is a multidisciplinary collection of physicians, research scientists, and health care providers at Duke University Medical Center who seek to improve the care of men living with prostate cancer. Our aim is to achieve this through a team approach by providing information and consultation at the time of diagnosis, providing state-of-the-art treatment options in urology, radiation oncology, and medical oncology, and in developing new treatments based on basic, translational, and clinical research. We are physically located on the second floor of the Duke Clinics in 2L, a new space dedicated to this multidisciplinary center.

Our research staff is dedicated to understanding the underlying causes of prostate cancer and how it progresses, and developing therapies based on these findings, including new surgical techniques, radiation techniques, active surveillance, and new medications directed at prostate cancer. Our goal is to allow men to continue living free of prostate cancer and the symptoms associated with this illness and its treatments.

## Duke Prostate Center

If you are interested in learning more about the Duke Prostate Center, please contact our Development Office at **919-667-2530**.

To make an appointment in the Duke Prostate Center, please contact Terry Witting at **919-668-8108**.

For other appointments or information on prostate cancer services at Duke, call the Duke Referral Center at **1-888-ASK-DUKE**. Representatives are available Monday through Friday, 7:30 a.m. to 6:00 p.m.

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