PCRP’s Commitment to Resolving Prostate Cancer Health Disparity

Prostate cancer (PCa) is a common disease with which 1 out of every 6 men will be diagnosed during their lifetime, and 1 in 36 men will die (http://www.cancer.org/Cancer/ProstateCancer/DetailedGuide/prostate-cancer-key-statistics). Predictions by the American Cancer Society estimate that in 2010 alone, approximately 217,730 men in the United States will be diagnosed with prostate cancer and 32,050 men will lose their life to this disease. Although men from any race, ethnicity, or socioeconomic group may acquire PCa, some populations are disproportionately affected. African American (AA) men are particularly vulnerable, with an increased risk of incidence and mortality more than twice that of any other ethnic group.

Since its inception in 1997, the Prostate Cancer Research Program (PCRP) has focused on identifying and funding innovative, high-risk/high-impact research aimed toward the prevention, detection, diagnosis, and treatment of human prostate cancer in all populations. The PCRP’s longstanding commitment to resolving prostate cancer health disparity has been evidenced by its

Landmark Consortium Wraps Up 8 Years of Data Collection and Investigation into Prostate Cancer Health Disparity

The Prostate Cancer Project (PCaP) Consortium was established in fiscal year 2002 (FY02) with a Consortium Award funded by the Prostate Cancer Research Program (PCRP)(1). Directed by Dr. James Mohler of the Roswell Park Cancer Institute (RPCI), and in collaboration with Dr. Jeannette Bensen at the University of North Carolina at Chapel Hill (UNC-CH), and Dr. Elizabeth Fontham at Louisiana State University Health Science Center (LSUHSC), the PCaP sought to evaluate multiple contributing
Research from either blood or mouthwash samples (RP) tissue blocks. DNA was processed from cells, urine, mouthwash, toe nail clippings, collected include plasma, serum, red blood cells, urine, mouthwash, toe nail clippings, and diagnostic and radical prostatectomy (RP) tissue blocks. DNA was processed from either blood or mouthwash samples for more than 98% of patients in the study, creating an unparalleled resource for prostate cancer health disparity research.

In addition, peripheral blood mononuclear cells are being immortalized in an effort to perpetuate this valuable resource. To date, 6,284 diagnostic blocks and 7,287 RP blocks have been processed although annotation of the samples is ongoing. Some of the tissue samples have been used to create tissue microarrays (TMAs), which permit the simultaneous analysis of hundreds of patients. More than 98% of patients have consented to continued follow-up, which will greatly increase the value of the annotated repository specimens.

Several epidemiological studies were conducted with the information gathered from the in-home interviews. One issue addressed was the interactions of these men with their health care provider. Interview responses showed that CA men placed greater trust in their physicians than AA men, likely because they were also more likely to visit the same physician on multiple visits, thereby increasing the likelihood of developing a trusting relationship.

Personal interactions and levels of trust in the care received were found to be important criteria in another study that examined satisfaction with the health care system. In another project, analyses are in progress to assess the results of a dietary questionnaire designed to establish the relationship between dietary intake and prostate cancer aggressiveness.

With the completion of sample collection, a number of genetic studies are now being conducted to compare the expression of genes and single nucleotide polymorphisms (SNPs) in AA and CA men with prostate cancer. One study is examining more than 1,500 SNPs in 2,000 men to determine whether there is a common polymorphism in AA men that affects disease severity and/or susceptibility.

Although analysis is ongoing, most of the SNPs identified as correlating with prostate cancer are unique to either AA or CA men but are rarely common to both groups. Another project has identified 40 novel SNPs not previously discovered by genome-wide association studies (GWAS), which have statistically significant differences in allelic frequencies between aggressive and nonaggressive prostate cancer. Yet another project is using a proteomics-based approach for biomarker discovery and aims to concentrate proteins that are present in low abundance but may be highly likely to be able to distinguish between prostate cancers and normal tissue and between different racial groups. Several candidate markers have been identified that are elevated before, but not after, prostatectomy.

The roles of androgen receptor (AR) and AR-regulated genes have also been examined by PCaP investigators since androgen levels trend higher in AA men. TMA analysis of 200 prostatectomy samples is under way to compare the expression of related genes. This will be accompanied by measurements of tumor growth rate in AA and CA men. The AR co-regulator melanoma antigen gene protein A11 (MAGE-11) is also a focus of interest, to determine if it is differentially expressed in AA and CA men or in aggressive and nonaggressive prostate cancer.

The depth of information contained in the PCaP data sets is just beginning to be realized. With the PCaP data sets finalized and quality-assured, the data and repository specimens have been made available (http://www.ncla-pcap.org/) for additional studies by the prostate cancer research community. Approval for use of the resources is dependent upon availability of desired samples or data, as well as scientific merit. Importantly, future studies using these data and specimens will finally provide definitive answers to the factors associated with prostate cancer risk, and especially those that are responsible for the disproportionate incidence and death rate of prostate cancer in African American men.

Cross-Cultural Studies of Prostate Cancer Health Disparity

Flora Ukoli, M.D., M.P.H.
Meharry Medical College

The disproportionate effect of prostate cancer on African American men compared to other ethnic groups is a sobering reality for any research investigator concerned with health and public health policy, given the approximately 60% higher incidence and twice the mortality rate compared to Caucasian men. Dr. Flora Ukoli, recipient of a PCRP fiscal year 1999 (FY99) Minority Population Focused Collaborative Award (MPFCA), FY01 Idea Development Award (IDA), FY04 HBCU Collaborative Partnership Award (HCPA), FY05 Clinical Trial Development Award (CTDA), and FY08 Collaborative Undergraduate HBCU Summer Training Program Award (STPA), has focused her investigations on the effects of diet and environmental factors on prostate cancer risk in African American and West African men, developing a prostate cancer program, and training young investigators in prostate cancer research. With her FY99 MPFCA she developed a pilot case-control study to examine the effects of dietary and lifestyle changes that affect prostate cancer risk in African migrants to the Washington, DC metropolitan area, compared to men in Nigeria. Using advertising in African cultural centers and business establishments to recruit participants, Dr. Ukoli conducted a case-control pilot study with a cohort of 11 West African men that included a dietary questionnaire, the collection of urine and blood samples, and other study instruments. Analyses of blood samples showed a high level of omega-6 fatty acids among African migrants living in the United States while Nigerian men exhibited higher levels of omega-3 fatty acids. These differences will be confirmed in a larger cohort study. Omega-3 and omega-6 fatty acids are essential for normal growth and health. The disproportionately high amounts of omega-6 in western diets compared to low amounts of omega-3 are thought to contribute to cancer, cardiovascular disease, and inflammation. Studies have shown a correlation between high intake of foods rich in omega-3, such as fish and fish oils, and reduced risk of prostate cancer.

Program News

- The PCRP received 1,027 compliant preproposals and 1,179 compliant applications for funding in FY10.
- Peer review for all award mechanisms was completed in August 2010. A total of 359 scientist reviewers and 70 consumer reviewers participated in PCRP peer review.
- Programmatic review for most award mechanisms will be conducted in October 2010 and funding status notifications provided in early November.
- Vision setting for FY11 will be conducted in November 2010.
- In FY10, PCRP staff members presented information on PCRP-funded research and new funding opportunities at the 8th World Basic Urological Research Congress, the AACR Annual Meeting, the AUA Annual Meeting, and educational summits of Us TOO International, ZERO: The Project to End Prostate Cancer, and the Prostate Health Education Network.
- For Prostate Cancer Awareness Month, the third issue of PCRP Perspectives has been released and special stories on PCRP-funded research and prostate cancer survivors are available at http://cdmr.army.mil/pcrp/.
- The next PCRP Innovative Minds in Prostate Cancer Today (IMPaCT) Meeting will be held March 9-12, 2011 in Orlando, Florida. The meeting will highlight progress in prostate cancer research supported by the PCRP and will serve as a forum to discuss critical issues and explore new avenues of research.
investment in a portfolio of studies that examines the interaction and impact of biological, genetic, socioeconomic, cultural, and environmental factors affecting prostate cancer risk. Through investments in individual investigators, multidisciplinary and multi-institution team science, and training opportunities for new young investigators, the program has supported health disparity research to better understand and potentially resolve disparities in AA populations. Numerous basic, translational, and clinical research projects focused on health disparity have been supported through various award mechanisms (Figure 1a), including the Health Disparity Research Award (HDRA), Health Disparity Training Award (HDTA), Idea Development Award (IDA), Synergistic Idea Development Award (SIDA), New Investigator Award (NIA), Exploration-Hypothesis Development Award (EHDA), Consortium or Consortium Development Awards (CA or CDA), Physician Research Training Award (PRTA), other training awards for pre- and postdoctoral fellows, Collaborative Undergraduate Historically Black Colleges and Universities (HBCU) Student Summer Training Program Award (STPA), HBCU Collaborative Partnership Award (CPA), and Minority Population-Focused Collaborative Training Award (MPCTA). To date, the program has supported over 146 awards totaling over $40.5M in its efforts toward resolving prostate cancer health disparity. The knowledge gained from these studies will help delineate the underlying causes of the high incidence and mortality due to prostate cancer in AA men.

The increased incidence and mortality of prostate cancer among AA men are thought to be associated with both genetic and socioeconomic risk factors. The PCRP has funded projects addressing both of these areas, as well as training and infrastructure projects that help to establish young investigators and new prostate cancer research programs (Figure 1b) in this field of research. The PCRP portfolio includes 59 projects focused primarily on the genetic and biological factors of health disparity, funded by 9 different award mechanisms, and 37 projects funded through 7 different award mechanisms that have primarily addressed socioeconomic differences between men of varying race, ethnic, and environmental/geographical backgrounds. Some of these projects addressed multiple categories.

Genetic and biological risk factors studied by PCRP award recipients include differences (1) at the genetic level (e.g., single nucleotide polymorphisms [SNPs], microRNA expression, use of different alleles or splice variants), (2) in the expression of various genes, (3) in blood or tissue hormone levels, (4) in the ability to absorb vitamin D, zinc, or other natural elements or compounds, (5) in the intake level or absorption of antibiotics and nonsteroidal anti-inflammatory drugs, red meat, dairy products, or dietary supplements, and (6) in the response to prostate cancer therapeutic interventions or short-term exercise. Many new differences in allelic frequency and gene or microRNA expression have been discovered, opening up new avenues of investigation and offering hope for new and more effective treatment options for populations of men disproportionately affected by PCa.

In addition to genetic and biological risk factors, PCRP-funded investigators are also investigating the socioeconomic risk factors associated with prostate cancer health disparity. Some of the projects include studies focused on the extent to which various populations (1) are aware of their prostate cancer risk, (2) understand the importance of prostate cancer screening, (3) trust and respect their health care providers, (4) have access to health care and health insurance, (5) have support from family members, and (6) are willing to make lifestyle changes. Also investigated were differences in physical activity level, tobacco use, diet and obesity, and the type of care desired and received. Several of these studies have shown that greater efforts are required to educate the general public, especially minority populations, on the importance of prostate cancer screening, risk factors, and informed decision making with regard to treatment options. In fact, it has been found by multiple investigators that the method of dissemination is often critical to successful outreach.

Finally, the PCRP’s commitment to resolving health disparities is exemplified in its 2002 support of one of the most comprehensive investigations into the biological and sociological factors that contribute to racial differences in prostate cancer incidence and mortality between AA and Caucasian men through the Prostate Cancer Project (PCaP) Consortium. This landmark study is nearing completion and its data will be analyzed in the coming months and years. It is anticipated that the findings from this study will conclusively answer some key questions, while generating others, and ultimately change public policies and clinical care standards, influence behavior, and have a more major impact toward resolving prostate cancer disparities. A more detailed discussion of the PCaP Consortium, its goals, accomplishments, and resources for collaboration and partnership is also presented in this issue of the newsletter.
Under her FY01 IDA, Dr. Ukoli expanded her investigations of fatty acids and antioxidants (vitamin E) to determine how these dietary nutrients affect cancer risk and whether migration impacts exposure to dietary risk factors for prostate cancer. Her expanded cohort included African Americans, migrant Africans in America, and Nigerians of similar socioeconomic status and age for both prostate cancer cases and controls. Dr. Ukoli found significant differences in omega-6, omega-3, docosahexaenoic (DHA), palmitic, stearic, and oleic acid among the ethnic groups. The African American group had the highest body mass index and highest mean total of omega-6 fatty acids, both of which were associated with prostate cancer cases. Migrant Africans and Nigerians showed the highest omega-3 fatty acids index (37.9%) and (36.9%), respectively, compared to 8% found in a small percentage (6.1%) of African Americans.

With the support of an FY04 HCPA, Dr. Ukoli developed a prostate cancer research and training program at Meharry Medical College with a research focus on prostate cancer health disparity in African American men. She collaborated with investigators at Vanderbilt University to train minority faculty and graduate students in prostate cancer research while conducting a case-control study to identify genetic and environmental factors that contribute to prostate cancer health disparities in African American men. Specifically, the studies were focused on assessing the role of lycopene, an antioxidant found in tomatoes, as a factor in prostate cancer progression in African American and Nigerian men, and determining whether the type II diabetes drug, thiazolidinediones, inhibits prostate cancer progression in cell studies in collaboration with Dr. LaMonica Stewart. In line with these plans and based on preclinical data that show a correlation between prostate cancer and diets high in animal fats and low in antioxidants, Dr. Ukoli designed a double-blind, randomized, controlled Phase II trial with funds from her FY05 CTDA to test the effects of lycopene-containing supplements in reversing prostate cancer progression in African American prostate cancer survivors with biochemical failure. Since African American men consume more animal fat and lower amounts of antioxidants compared with groups with lower prostate cancer risk, this type of study could lead the way toward a specific intervention in this high-risk population.

With her most recent award, an FY08 STPA, Dr. Ukoli is creating opportunities for undergraduates from nearby Fisk University to train in prostate cancer. Through this new collaboration, forged with Dr. Shirley Rainey at Fisk, and existing ties with Vanderbilt University, Dr. Ukoli is able to provide mentoring and training for students in prostate cancer biology, epidemiology, and behavioral health. Students chosen through a competitive selection process participate in an intensive 12-week didactic curriculum that includes seminars, journal clubs, grand rounds, workshops, community networking, and training in laboratory techniques, data collection, and data management. The students have the opportunity to interact with scientists and clinicians through individualized research projects that extend beyond their time at Meharry College of Medicine and continue throughout the academic year, resulting ultimately in a completed manuscript for publication and attendance at a national conference. This experience is meant to encourage the summer interns to consider a career in prostate cancer research and to perpetuate, in other minority students at Fisk University, an interest in biomedical science careers.

Dr. Ukoli has used her expertise in preventive health, epidemiology, and prostate cancer research and her experience in training undergraduate and graduate students to advance the understanding of prostate cancer health disparity and the progress of prostate cancer research and to help mold the future generation of prostate cancer researchers. With funds from the PCRP, she has opened new avenues of investigation that may uncover the factors contributing to the disproportionate burden of prostate cancer on African American men. Her efforts are contributing to a new understanding of the disease and may influence health behavior and affect public health policy.

Did You Know...

Over 217,730 men in the United States will be diagnosed with prostate cancer this year.

The PCRP has provided support to over 2,256 scientists with over 2,000 awards. Of these, 92 awards went to 41 international institutions outside of the United States representing 11 different countries. The reach of the PCRP demonstrates its commitment to ensuring that the best ideas in prostate cancer are supported in prostate cancer research.

In fiscal year 2010, the PCRP took unprecedented steps to address the problem of overtreatment of prostate cancer, declaring as one of its Overarching Challenges the effort to distinguish lethal from indolent disease and creating the Impact Award, which is specifically designed to fund only projects with significant potential to reduce or eliminate overtreatment.

Us TOO International is one of the largest prostate cancer patient advocacy, education, and support organizations in the world with over 325 chapters. In 2010, Us TOO celebrates its 20th anniversary of helping men and their families in making informed decisions about their prostate health and treatment. Us TOO was formed in 1990 by five men who were diagnosed and treated for prostate cancer. Today, Us TOO has gained international prominence through its effective leadership and outstanding organizational and community-based efforts, all of which led to its being granted membership in the National Health Council.
When writing a training plan, in addition to describing how to minimize, and ultimately eliminate, search and training mechanisms that work disparity through specifically targeted re-
the efforts of the PCRP to combat health newsletter are only a small sample of and other highlights in this issue of the bilt University to train the next generation collaborating with investigators at Vander-
Ukoli is also maximizing PCRP support by progression in African American men. Dr. Flora Ukoli of Meharry Medical College, type II diabetes drugs in prostate cancer risk factors associated with prostate cancer. These, and other highlights in this issue of the newsletter are only a small sample of the efforts of the PCRP to combat health disparity through specifically targeted re-
search and training mechanisms that work to minimize, and ultimately eliminate, prostate cancer’s impact on Black men, their families, and their communities.

As an African American man and a prostate cancer survivor of 15 years, I know the fear, anguish, uncertainty, and physical results of the disease. However, as a patient advocate and member of the PCRP Integration Panel, I also believe in the importance of aggressive research, and I know that the PCRP represents our nation’s best efforts to find a cure for prostate cancer.

As the PCRP strives to realize its vision of conquering prostate cancer, we must all redouble our efforts to understand the disease by educating ourselves and our communities about prostate cancer risk. We must act to protect ourselves and our family members through early detection, lifestyle and dietary changes, and active participation in the research process (both clinical and basic). We must be the change that eliminates prostate cancer!

Visit the PCRP Webpage for Up-to-Date Program Information

The DOD Prostate Cancer Research Program (PCRP) supports innovative ideas and technologies to accelerate our vision to conquer prostate cancer through individual, multidisciplinary, and collaborative research. These efforts are focused toward basic research discoveries and translating discoveries into clinical practice to improve the quality of care and life of men with prostate cancer. For more information on PCRP initiatives, highlights of funded research, and consumer profiles, please visit the PCRP webpage at http://cdmrp.army.mil/pcrp/default

To subscribe to this free newsletter, please contact the editor at perspectives@cdmrp.org.