Meeting Report of the 29th Annual International Symposium of the Center for Translational and Basic Research (CTBR) in partnership with Weill Cornell Clinical and Translational Science Center (CTSC)

CURRENT ADVANCES IN PROSTATE CANCER HEALTH DISPARITIES

The full-day symposium took place on Thursday, May 5, 2016
The Kaye Playhouse at Hunter College of CUNY
Overview

Prostate cancer is the most frequently diagnosed non-skin cancer in men in the western world. A subset of prostate cancer is very aggressive, and often results in death. The incidence and mortality rates of prostate cancer is highest among men of African descent. Hunter College's Center for Translational and Basic Research (CTBR), along with Weill Cornell Clinical and Translational Science Center (CTSC), chose to focus the 29th Annual International Symposium on this profound public health problem.

Introduction

Joseph Osborne, MD, PhD, an Assistant Member and Associate Vice Chair Research at Memorial Sloan Kettering Cancer Center, began the day's proceedings by quoting the Reverend Dr. Martin Luther King, Jr. “Of all the forms of inequality, injustice in health care is the most shocking and inhumane,” Dr. King said in a speech he gave to the Medical Committee for Human Rights at their annual meeting in Chicago in 1966. Osborne agreed with Dr. King's assessment, and noted that current science should be able to eliminate inequalities in health care access, quality, and outcomes.

Osborne mentioned that he has relatives who have survived prostate cancer and relatives who have succumbed to it, and spoke of how personal the day therefore was to him. He was looking forward to hearing the new insights and opportunities it would reveal about how to help African American men, who have double the risk of prostate cancer as white men. And he noted that the social justice aspect of conquering this cancer health disparity cannot be divorced from the medical aspect.

Philip Kantoff, the Chairman of the Department of Medicine at Memorial Sloan-Kettering Cancer Center, was the first keynote speaker of the day. He spoke of the paradox of prostate cancer, which is similar to that for other cancers; the double edged sword of overtreating those with indolent cancers who do not need it to try to catch those with aggressive cancers who can benefit from it. To avoid overtreatment, he said we must find better molecular markers for aggressive disease. He vehemently disagrees with the United States Preventative Services Task Force recommendation of 2012 against PSA-based screening for prostate cancer regardless of age, race, and family history. This sentiment was echoed by all of the other speakers over the course of the day.

Next was a panel discussion featuring Kantoff; Curtis Pettaway, a Professor of Urology at the University of Texas MD Anderson Cancer Center; Brian Harper, the Medical Director of Academic Health Centers at the College of Osteopathic Medicine, NY Institute of Technology; and Reverend Patrick H. O'Connor, the Lead Pastor of First Presbyterian Church, a multicultural congregation in Jamaica, Queens. O'Connor was
the only prostate cancer survivor to speak, and thus brought the much valued patient’s perspective to the symposium. Harry Belafonte was scheduled to be on the panel as well, but could not be there due to health issues.

The afternoon’s speakers reiterated many of the themes addressed in the morning sessions, specifically that (1) social and economic factors contribute to black men’s two fold higher incidence of prostate cancer incidence and mortality and therefore must be addressed along with medical factors and (2) black men should ignore the United States Preventative Services Task Force recommendation and get PSA tests, even as young as at age 35.

Curtis Pettaway delivered the afternoon’s keynote address, in which he outlined the misguided nature of the United States Preventative Services Task Force recommendation and implored all men of African descent to be screened for prostate cancer. Folakemi Odedina spoke of her work trying to understand the experiences that black men endure at the moment they are diagnosed with prostate cancer. Timothy Rebbeck spoke of the cultural factors at play in health disparities, and their interactions with biological factors. Hunter’s own Olorunseun Ogunwobi described his work in trying to identify additional biomarkers to be used in prostate cancer diagnosis, and Douglas Scherr concluded by outlining the progress urologists have made in stratifying patients by risk and therefore only performing surgery on those men who need it.

**Sponsorship**

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The Paradox of Prostate Cancer

Speaker:

Philip W. Kantoff, MD, Chairman of the Department of Medicine, Memorial Sloan-Kettering Cancer Center

Highlights:

- The paradox of prostate, and really all, cancers: the double edged sword of overtreatment and mortality.
- Men of African ancestry are more than fifty percent more likely to be diagnosed with prostate cancer than white men. They are twice as likely to die of the disease. These disparities have social as well as biological causes.
- In addition to the androgen receptor gene, genome wide association studies have identified over 100 single nucleotide polymorphisms that are associated with a slightly increased risk of prostate cancer.
- As yet, there is no chemopreventive strategy effective against prostate cancer.

The paradox of the title was laid out in the early 1980s by Willet Whitmore, who served as chief of urology at what is now Memorial Sloan-Kettering Cancer Center from 1951 through 1984. Whitmore said: “Is cure necessary in those for whom it is possible, and is cure possible in those for whom it is necessary?” Even then he recognized the double edged sword of overtreatment and mortality that still plagues the field of oncology. There are patients for whom cure is not necessary, but who still receive treatments that are physically, psychologically, and financially debilitating; but there are also those with lethal cancers that are recalcitrant to known treatments. The key is being able to distinguish between the two groups.

Health Inequities

Men of African ancestry are more than fifty percent more likely to be diagnosed with prostate cancer than white men. They more likely to be diagnosed at a later stage of the disease; they are treated differently; and they respond to treatment differently. These disparities have social as well as biological causes. African men are more likely to be diagnosed at a later stage of the disease partially because it strikes them earlier, and partially because their culture has not promoted early and vigilant surveillance (although that is changing).

Genetic Factors

The androgen receptor gene is found on the X chromosome. It can have a variable number of CAG repeats in different men. Each of these repeats encodes a glutamine residue at the N-terminus of the protein, and fewer of these repeats make a stronger receptor that binds to androgens like testosterone more tightly. Men of African ancestry tend to have fewer of these repeats than Caucasian or Asian men, rendering their receptors hypersensitive to testosterone. Data from the Physicians’ Health Study, a cohort study carried out from 1982-1995, indicates that men with fewer of these repeats have a fifty per cent higher rate of metastatic, high stage, fatal prostate cancer. This finding was confirmed with case control studies of men after their diagnoses.
Prostate cancer is the most heritable cancer there is, as shown in twin studies. In addition to the androgen receptor gene, genome wide association studies have identified over 100 single nucleotide polymorphisms that are associated with a slightly increased risk. The HOX B13 gene, important during development, is a bona fide susceptibility gene; mutations in it yield a 20 fold increased risk, but they are rare. Mutations in the tumor suppressors PTEN and p53 and the transcription factor ETS are also known to contribute to prostate cancer, although it is not yet known precisely how. A recent multi-institutional undertaking to understand the genetic drivers of advanced prostate cancer sequenced exomes from a hundred and fifty biopsies and revealed the surprising finding that about thirty percent of them harbored DNA repair abnormalities, like those in BRCA1 and BRCA2, that are more often thought to be associated with breast and ovarian cancers.

Treatment Options

A recent retrospective analysis of thousands of men with prostate cancer revealed that black patients with the disease were thirty percent less likely than whites to undergo radical prostatectomy within the first three months after their diagnosis. This surgery is currently the standard of care to prevent death. They also had a 7-day treatment delay compared with non-Hispanic whites. Black patients were less likely to undergo lymph node dissection; but when they did have surgery, they suffered higher odds of postoperative visits to the emergency department and readmissions compared to non-Hispanic whites. Their surgeries were also associated with a higher incremental annual cost. Despite these treatment differences, this study did not find a difference in mortality between black and non-Hispanic white men with prostate cancer. However, it only followed the men for a year after their diagnosis.

As yet, there is no chemopreventive strategy effective against prostate cancer. In the 1990s there was data suggesting that antioxidants like vitamin E and selenium might be protective, but the SELECT trial demonstrated that the opposite was in fact the case. Studies on 5-alpha reductase inhibitors like finasteride and dutasteride, which inhibit the conversion of testosterone into the more potent dihydrotestosterone within the body, have yielded conflicting results. Some have suggested that the drug reduces the incidence of prostate cancer; but those men that do develop it were more likely to have a higher grade. The FDA has opted not to approve these drugs.

Screening and Mortality

Based on three different studies published in 2012, the United States Preventative Services Task Force recommended against PSA-based screening for prostate cancer regardless of age, race, and family history. Kantoff, along with all of the other speakers at the day’s symposium, could not disagree more strongly. At least one of the studies on which the recommendations are based were severely flawed because most of the men in the control group who were supposed to forego screening got screened anyway. The other two indicated that either twelve or thirty-seven men need to get treated to prevent one death.

While admitting that over treatment is a problem, Kantoff still thinks that eliminating screening is the wrong conclusion to take from these studies. He pointed out that
screening has lowered the age of men who are diagnosed as well as the stage at which tumors are found; thus, it is identifying the most advanced cancers, those endangering the lives of the very patients who can most benefit from treatment. Mortality from prostate cancer had fallen 25% because of PSA screening, but has crept up again since these recommendations were made.

Rather than eliminating screening, he thinks, we must make sure to screen those who are at high risk – men of African ancestry – and concentrate on better identifying those with advanced disease (defined by a Gleason score of 8-10) who can most benefit from treatment. Thus far, the only randomized controlled trial in the US that compared treatment (radical prostatectomy) to observation (watchful waiting or active surveillance) found no decrease in mortality due to treatment except in the highest risk patients.

References

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Bill-Axelson et al. Radical prostatectomy or watchful waiting in early prostate cancer. NEJM 2014 Mar 6; 370(10)939-42.


PANEL DISCUSSION

Panelists:

● Philip W. Kantoff, MD, Chairman of the Department of Medicine, Memorial Sloan-Kettering Cancer Center
● Curtis A. Pettaway, MD, Professor of Urology, University of Texas, Anderson Cancer Center
● Brian L. Harper, MD, MPH, Medical Director, Academic Health Centers, College of Osteopathic Medicine, NY Institute of Technology
● Reverend Patrick H. O’Connor, Lead Pastor, First Presbyterian Church (Prostate Cancer Survivor)

Moderator:

Bert M. Petersen, Jr., MD, Director of the Breast Surgery Clinic Program, St. Barnabas Hospital

Highlights:

● Everyone who spoke at the symposium disagrees with the United States Preventative Services Task Force recommendation against PSA-based screening for prostate cancer; it is not appropriate for black men.
● However, screening is not enough; appropriate follow up and treatment are also required, and the infrastructure to provide them should be put in place before a screening program is initiated.
● Unemployment and poverty are major determinants of poor health outcomes, and these social needs must be met as medical needs are being addressed.
● Many black men are treated condescendingly by doctors and are therefore somewhat distrustful of the medical system as a whole.
● To induce the African American community to participate in clinical trials it is essential to get women involved, because even though they don’t get prostate cancer they wield enormous influence in their matriarchal culture. Faith based organizations must be engaged as well.

Philip Kantoff started the panel discussion by reiterating some of the themes he touched on during his keynote. As the PSA test became widespread, starting in 1991, it ushered in a new era for urologists. Since it allowed prostate cancer to be detected molecularly before a physician could physical palpate it, urologists were doing tons of biopsies and radical prostatectomies. It took time for randomized, controlled studies to be done to determine the test’s effect on mortality. Now that those studies have been done, they show that the PSA test can in fact reduce mortality. But there has been a backlash against it because so many men are being needlessly treated for indolent cancers. He also insisted that more cancer patients, including black cancer patients, must participate in clinical trials to make progress in medicine that can possibly help them and certainly help the rest of society.
Curtis Pettaway noted that screening is not enough; appropriate follow up and treatment are also required, and the infrastructure to provide them should be put in place before a screening program is initiated. Men of African descent in the US still need to be educated about prostate cancer and the PSA test, which is beginning to happen. Hopefully they will serve as models for men in the Caribbean and in Africa. Like Kantoff, he vehemently disagrees with the United States Preventative Services Task Force recommendation against PSA-based screening for prostate cancer. Men of African descent get prostate cancer about five years earlier than white men, and it is often more metastatic and aggressive. Rather than eliminating screening, he suggests alleviating the problem of overtreatment by refining the screen. To do this, researchers must find additional molecular markers for aggressive disease.

Brian Harper aims to raise the education level of the black community about PSA screening and clinical trials. As part of the Harlem Men’s Initiative, he involved the NBA in screening programs at the Ralph Lauren Center for Cancer Care to incentivize other men. Al Sharpton got screened, as did Anthony Mason, Kareem Abdul-Jabar, LeBron James, Will Frasier, and other prominent athletes, journalists, and jazz musicians. Harper was also the first to mention that unemployment and poverty are major determinants of poor health outcomes, and these social needs must be met as medical needs are being addressed.

Patrick O’Connor was the only prostate cancer survivor to speak at the symposium. He is the Lead Pastor and “Chief Visionary” of First Presbyterian Church, a multicultural congregation in Jamaica, Queens. Many worshippers there work at nearby Jamaica hospital where they watch men of African descent in their 50s being treated for aggressive prostate cancer. One such worshipper encouraged Mr. O’Connor to get screened, telling him to specifically ask his doctor for a PSA test or he wouldn’t get it. He asked for the test when he was 37, and his doctor refused; he persisted, leading to his diagnosis at age 40. He noted that it took him a while to find a doctor he liked and trusted, Douglas Scherr, who he then induced to run a screening program in the church. Many black men had been treated condescendingly by doctors – as he himself was – and were therefore somewhat distrustful of the medical system as a whole. Running screening out of the church lent credibility to the screening initiative, which includes a lecture, time to talk to Dr. Scherr, an option to follow up with him or another urologist, and has now expanded to include screening for diabetes, hypertension, and glaucoma.

**Questions and Answers**

The first question came from Michael Garner, the president of the New York City chapter of One Hundred Black Men. He asked Dr. Pettaway if he thought black men should get their first PSA test at age 35 or 45. Pettaway answered that the incidence of prostate cancer does start to rise around age 45, but that it is useful to have an earlier
baseline PSA possibly around age 40 and also to measure changes over time, This can be a predictor of how aggressive a later cancer might be.

Bert Peterson asked if there are any other markers besides PSA that could be used for screening. Drs. Kantoff and Pettaway both lamented that there are none yet proven; some are desperately needed to distinguish aggressive cancers that require instant treatment from indolent cancers that will allow the men who harbor them to die of other causes.

A man in the audience said he was 70 and his PSA has been hovering around 4 for years; he has had one biopsy and his urologist advised watchful waiting. He wanted to know if there were any vitamins he should be taking. Pettaway said that his urologist knew him best, and he should heed his doctor’s counsel. He also said that a multivitamin is fine, but that the man should not take any other vitamins or supplements, like saw palmetto. Rather, he should stick to a heart – and prostate – healthy lifestyle: exercise, maintain a healthy weight, don’t smoke. Kantoff added the he should make sure he had adequate vitamin D – not just for his prostate, but for overall health.

The next questioner wondered how the medical establishment could induce people of color to participate in clinical trials. Peterson insisted that it must get to know and understand the particular population they are targeting. To engage the African American community it is essential to get women involved, because even though they don’t get prostate cancer they wield enormous influence in their matriarchal culture. Faith based organizations must be included as well. Kantoff added that the community must be educated about what the trials are, what participation entails and what they aim to accomplish – and that they may also need access and transportation to trial sites. O’Connor noted that community members need to talk more about this amongst themselves – he didn’t even know he had a family history of prostate cancer until after he began treatment.

The last questioner wondered why the PSA test doesn’t reduce mortality as much as screening for colon cancer decreases mortality from that disease. The doctors on the panel said that PSA screening does reduce mortality, but that men with highly aggressive (Gleason 8-10) prostate cancers can die from them despite our best treatment. And of course, the biology of each type of cancer is different.
The Need for Prostate Cancer Early Detection Among Men of African Descent: Why the United States Preventive Services Task Force Recommendation is Potentially Harmful!

Speaker:

Curtis A. Pettaway, MD, Professor of Urology, University of Texas, Anderson Cancer Center

Highlights:

- The United States Preventative Services Task Force recommendations are not relevant to men of African descent.
- At least six biomarkers for prostate cancer are differentially expressed in men of African descent as compared to Caucasian men.
- A PSA of 1.5ng/ml was a good cutoff for increased cancer risk in one study.
- Morbidity and overtreatment of prostate cancer can be reduced through clinical trials and the identification of additional molecular markers to risk stratify patients; not through eliminating screening.

Men of African descent with prostate cancer are twice as likely to die from it as other men. Like all of the day’s speakers, Curtis Pettaway wants to better understand this disparity in order to eliminate it. He went through the biological and social causes of this inequality that are known thus far, and concluded by insisting that much of this mortality can be, and in fact has already been, abated by screening with the PSA test.

Biases, Genetic and Otherwise

Pettaway started by noting that there are certainly biases in the treatment options offered to black patients, and in those they accept. Studies have shown that black men are offered radical prostatectomy, the most effective treatment for aggressive prostate cancer, less frequently than white men. But there are also real biological risk factors to account for the discrepant toll prostate cancer takes on black men.

Out of at least twenty that have been examined, there are at least six biomarkers for prostate cancer that have been identified thus far that are differentially expressed in men of African descent as compared to Caucasian men. One of these is for the androgen receptor. Loss of function mutations in two tumor suppressor genes predicted the risk of pathologic prostate cancer specifically in men of African descent. Dysregulation of three other genes was able to predict clinical outcomes, including 3-year biochemical recurrence and metastasis at 5 years. And a greater proportion of men of African descent were found to harbor simultaneous mutations in three of the markers as compared to Caucasian men.
The PSA era

The incidence of prostate cancer is the highest in developed countries, but mortality is highest in West Africa, South America, and the Caribbean – areas where there are a lot of men of African descent, but where screening with the PSA test is not a part of routine medical care, so they only get diagnosed with prostate cancer once the disease is in an advanced stage when it is often too late to treat successfully. This fact alone speaks to how much the PSA test has reduced mortality in the US. Pettaway, like all of the day’s speakers, insists that black men ignore the United States Preventative Services Task Force recommendation to skip PSA testing.

Pettaway said that a PSA of 1.5ng/ml was a good cutoff for increased risk. He also said that it is nice to have an early baseline so that trends can be discerned. Early detection of prostate cancer remains an effective way to reduce advanced disease and mortality, and may even eliminate health care discrepancies. Morbidity and overtreatment can be reduced through clinical trials and the identification of molecular markers, such as those described above, that can be used to risk stratify patients into those that require treatment and those that can be relegated to active surveillance. Eliminating PSA screening is not the way to reduce morbidity and overtreatment in men of African descent.

References

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Global Disparities in Prostate Cancer: From Nucleotide to Neighborhood

Speaker:

Timothy R. Rebbeck, PhD, Harvard TH Chan School of Public Health, Dana Farber Cancer Institute

Highlights:

- Race is a social, cultural, and historic construct as well as a biological one, as evidenced by the fact that it can change with time and place.
- Three genes that confer susceptibility to prostate cancer are more prominent in men of African ancestry because they “hitchhiked” along with the beneficial genes next to them before the slave trade created the African diaspora.
- The social components of one’s racial identity – culture, environment, behavior – are correlated with the biological components, like phenotypes, ancestry, and even genomic variation.

Timothy Rebbeck wants not just to understand, but to eliminate the two-fold disparities in prostate cancer incidence and mortality suffered by men of African descent – the largest disparity of any cancer in the United States. To that end, he aims to explore population and evolutionary genetics in this population; to identify any factors associated with prostate cancer etiology and outcome in this population; to evaluate the impact of higher level biological and social determinants of prostate cancer, and in particular of aggressive prostate cancer; and to develop the capacity to perform cancer research in Africa.

From Nucleotide…

Epidemiological studies often incorporate data about race, ethnicity, and ancestry, and much of this data relies upon self-identification. But Rebbeck pointed out that race is a social, cultural, and historic construct as well as a biological one, as evidenced by the fact that it can change with time and place. And of course there is much heterogeneity even within racial groups. It thus has limited utility – it cannot really define which individuals will develop aggressive disease, which we need to do to improve outcomes. Race is only a crude measure of which men are at highest risk.

When genetic risk factors congregate in a particular group of people, geneticists often speculate that they are also conferring some sort of benefit – that they have been selected for, so they remain in the genome despite the harm they do rather than getting
weeded out. Could this be the case for the genetic risk factors for prostate cancer harbored by men of African ancestry?

Rebbeck highlighted three chromosomal regions that have genes associated with prostate cancer in men of African ancestry, and said that the selection probably happened in Africa, before the slave trade took East Africans to what is now Brazil and dispersed West Africans all over the Americas and the Caribbean. These susceptibility genes “hitchhiked” along with the genes that were next to them, which were the ones selected for because they conferred favorable traits. One of these genes, on chromosome 2, is for pigmentation; another, on chromosome 7, is associated with reproductive fitness; and the last, on chromosome 19, protects against African eye worm infection.

Some biomarkers differ by race. The TMPR552-ERG2 fusion protein, for example, is much more prevalent in prostate cancers from Caucasian men than in men of African ancestry. And some genetic markers even seem to have opposite effects; higher expression of the ERG protein acts protective in African American men but is a risk factor for prostate cancer in European American men. Rebbeck noted that just because the genetic risks for the disease don’t work the same, that doesn’t mean the biology isn’t the same.

…to Neighborhood

The social components of one’s racial identity – culture, environment, behavior – are correlated with the biological components, like phenotypes, ancestry, and even genomic variation. These factors all interact to impact one another, and all of them can impact disease and outcome. So all of them must be targeted by prevention and treatment strategies.

In Philadelphia, Rebbeck and his colleagues parsed out the environment and culture of different neighborhoods and correlated them to the percentage of the local population’s genome that is African. They found that areas with people whose genomes were more “African” had lower levels of education and income, and higher levels of unemployment and poverty. He attributes this finding to segregation and discrimination, but it highlights that the differences between black and white men are not only biological. An audience member reiterated that poverty is a major source of stress, which is a risk factor for a large number of diseases.

Rebbeck concluded by noting that there must be something we can do to move beyond race, to understand what underlies these racial disparities and help all the men at risk.
References


Harries et al. Alterations in LMTK2, MSMB, and HNF1B gene expression are associated with the development of prostate cancer. BMC Cancer 2010 June 22; 10:315.


Point of Prostate Cancer Diagnosis (PPCD) Experiences & Needs of Black men: The Florida CaPCaS Study

Speaker:

Folakemi T. Odedina, PhD, Professor, College of Pharmacy and College of Medicine Director of Diversity, CTSI Translational Workforce Development Program, University of Florida

Highlights:

- Black men are a diverse group, with different physical, emotional, and financial backgrounds; they thus have different experiences and needs upon diagnosis with prostate cancer.
- By interviewing different groups of prostate cancer survivors, the CapCas study can provide a framework for physicians and community leaders to provide black men with their individualized needs at the point of diagnosis with prostate cancer.

Folakemi Odedina wants to understand the black man’s journey from prevention, to the life changing event of hearing “you have prostate cancer,” all the way through treatment, and hopefully into survivorship and, ultimately, advocacy. Black men are diagnosed with, and die from, prostate cancer at about twice the rate of white men. Over 30,000 black men are diagnosed with the disease annually, but there has been very limited research into their experiences and coping mechanisms, especially at the moment they receive their diagnoses.

CapCas Methodology…

As Odedina pointed out, in this context “black is not black;” black men are hardly a homogenous group. She and her team aimed to explore the experiences and economic, physical, psychological, and social needs of this diverse group in order to develop a model of care and survivorship. To that end, they culled through the 10,818 records of black men diagnosed with prostate cancer between 2006 and 2010 from the Florida Cancer Data System Registry. From these, they focused on 212 survivors. Seventy one percent were born in the United States; twenty-five percent were born in the Caribbean, primarily Jamaica, Haiti, and Guyana; and four percent were born in Africa. They then did in depth audio and video interviews with twenty men from each of these three groups. They spent about six hours with each man they interviewed.
...And Results

On the whole, they found that many of these black men make treatment decisions based on finances, on what their insurance will cover, or on if they have insurance at all. Many of them were not especially savvy in terms of health and healthcare, and were even distrustful of their doctors and the entire medical establishment. As a result, they often felt somewhat blindsided by their diagnosis. Others expressed the expected reactions of fear, disbelief, shock, fatalism, denial, and eventually, acceptance, resignation, resilience, and the urgent desire to take control.

A number of men spoke of feeling alone at the point of diagnosis. Unfortunately, some also perceived their doctors treating them with contempt, or in a sterile or even dehumanizing manner; certainly not displaying much empathy. If the doctor was black too, this perception was totally mitigated.

Some of the patients expressed a need for social support, because although prostate cancer is prominent among black men even those with a family history often do not talk about it. Odedina is therefore writing a grant to provide instant intervention for these men at the point of diagnosis, when they most need it and can most benefit from it.

References

http://epi.grants.cancer.gov/captc/
PVT1 Non-Coding RNAs in Prostate Cancer

Speaker:

Olorunseun O. Ogunwobi, MD, PhD, Associate Professor, Hunter College, City University of New York and symposium planning committee chair

Highlights:

- PVT1 exon 9 is overexpressed in aggressive prostate cancer cells from men of African ancestry, so might be a viable biomarker for this disease.
- miR-1207-3p is underexpressed in prostate cancers from men of African ancestry, but might likewise serve as a biomarker.

Olorunseun Ogunwobi maintains that the two-fold greater incidence and mortality in men of African ancestry compared to white men cannot be fully explained by lack of access to care or socioeconomic factors. Thus, one focus of his lab in Hunter’s Center for Translational and Basic Research is investigating the biological mechanisms underlying the racial disparities in specific solid cancers.

PVT1 exon 9

Genome wide association studies are used to identify stretches of DNA that are associated with susceptibility to a particular disease. Such studies have linked a region on chromosome 8q24 with susceptibility to prostate cancer; this region is in fact associated with highly aggressive prostate cancer in men of African ancestry. This region contains only one gene, which encodes the known oncogene c-Myc. This region contains the 300 kb long non-coding PVT1 gene locus.

Ogunwobi’s lab measured the levels of twelve of PVT1’s exons in eight different prostate epithelial cell lines and found that the expression of exon 9 is upregulated by about two fold in aggressive prostate cancer cell lines derived from men of African ancestry compared to both indolent prostate cancer cell lines derived from men of African descent as well as both indolent and aggressive prostate cancer cell lines derived from Caucasian men. Silencing PVT exon 9 resulted in cell cycle arrest, so its abundance might spur cell growth. PVT1 exon 9 was detectable in cell culture medium, suggesting that it is secreted from cells. If it is likewise detectable in urine or blood, perhaps it can be used as a diagnostic marker for aggressive prostate cancer, one that physicians can track during a period of active surveillance.
miR-1207-3p

Six microRNAs (miRNAs) are expressed from the PVT1 locus. One of these, miR-1207-3p, has the opposite effect of exon 9; miR-1207-3p serves to slow cell growth by inhibiting cell cycle progression. miR-1207-3p also regulates Fibronectin type III domain containing 1 (FNDC1). Prostate cancer patients of African ancestry have less of this miRNA than white patients do, so it might also become a diagnostic marker. It is found at comparable levels in indolent and aggressive prostate cancer cells derived from black men, suggesting that it is lost during the early stages of tumorigenesis.

More effective early detection and therapeutic strategies are required to decrease the two-fold disparity in the incidence of and mortality from prostate cancer that black men endure. These two specific markers, pulled out of the large region of chromosome 8q24 that had previously been linked to prostate cancer, may get us further towards that goal.

References

Das DK et al. miR-1207-3p as a potential prostate cancer biomarker in Black males. Cancer Epidemiol Biomarkers Prev March 2016 35; B02.

A Decade of Robotic Surgery: The Evolving Role of Robotic Prostatectomy in the Age of Active Surveillance

Speaker:

Douglas Scherr, MD, Professor of Urology, Director, Urologic Oncology, Meyer Cancer Center, Weill Cornell Medicine-NY Presbyterian Hospital

Highlights:

● PSA screening has reduced mortality and is essential, especially for men of African descent.
● Risk stratified screening is the way to avoid needless overtreatment of indolent cancers, and urologists have made great strides towards it in the past decade.
● Active surveillance is a viable option for low risk, reliable patients, but must be used more cautiously with higher risk patients.
● MRI guided biopsies have improved the identification of significant cancers.
● Robotic surgery has become indispensable in treating advanced disease.

Prostate cancer is still the most common cancer in men in the US today. Like the speakers before him, Douglass Scherr noted that the disparity in outcomes between black and white patients with prostate cancer is not due to biology alone, and stressed that the United States Preventative Services Task Force recommendation against PSA screening is tragically misguided. He did, however, appreciate the Task Force’s desire to avoid needlessly treating indolent cancers, and reviewed urologists' efforts and progress toward that goal.

Risk Factors and Screening

Having African ancestry is definitely a risk factor for prostate disease. But Scherr noted that it is a complex disease, and race doesn't explain the whole story. As we better understand the genetics and epigenetics of the disease, we can move towards personalized, individualized treatments.

Lifestyle factors can confer risk, and they can be race related just as biological factors can. Scherr spoke of the rise of obesity among Americans as a whole and among black men in particular, and pointed out that smoking rates are also high in this group. Adipose tissue has a lot of inflammatory, oncogenic properties, and thus increases one's risk of cancer much like smoking does. Now, doctors are looking at organ specific obesity, and looking at adipose tissue surrounding the prostate can help them assess a man’s risk of developing prostate cancer.
Few biomarkers have reduced the level of cancer mortality as much as PSA. Since screening became widespread, there has been a 39% reduction in death from prostate cancer and a 20% reduction in death from all cancers in men. The United States Preventative Services Task Force recommended against routine screening with the PSA test based on one study, the PLCO study, whose methodology was severely flawed; over 90% of men in the control group – those who allegedly were not screened – had in fact been screened. No wonder, then, that there was no difference in outcome between them and the group that was screened! And as if that weren’t bad enough, at most 4% of the men in this particular study were of African descent. All of the other studies showed a clear decrease in mortality from prostate cancer after the adoption of the PSA test. This recommendation is a real problem, because there are already too many black men who are not being screened simply because of a lack of education. If they don’t have symptoms, and are unaware of any family history, they don’t realize they are at risk.

This is not to say that there are no issues with screening. There is a lot of ambiguity in interpreting results, and doctors are also seeing more cases of less advanced prostate cancer since the PSA test became standard practice.

**Changes in Treatment**

In response to this recommendation, and to try to mitigate the negative physical, emotional, psychological, and financial effects of treating indolent cancers that don’t need to be treated, urologists have instituted a number of measures. All told, they have reduced the detection of low risk (Gleason 3+3) tumors by 17%, and of biopsies by 32%.

The first step they took was to stratify screening programs by risk. Rather than just measuring PSA levels, they now look at the different isoforms of PSA in plasma as well as a panel of 232 single nucleotide polymorphisms (genetic markers associated with prostate cancer). They also incorporate clinical factors like the patient’s age, family history, previous PSA levels, and the results of a digital rectal exam into the risk analysis.

Next, they have increased their use of active surveillance, which differs quite a bit from watchful waiting. Active surveillance is in fact quite active, so it is only suitable for a low risk patient who is also a reliable, responsible one. Men on active surveillance go to their doctors for a PSA test, digital rectal exam, and an MRI every six months; they get biopsied every year. The use of MRI to guide these biopsies has helped doctors identify which cancers are aggressive and require surgery. Molecular imaging, using radiolabeled antibodies or small molecules targeted to suspicious lesions in the prostate, has helped as well.
In 2004, robotic surgery accounted for only 10% of radical prostatectomies. In 2014, that number had jumped to 90%. Most surgeries are now done only on high risk patients, as the field has moved away from treating tumors with a grade of Gleason 6 or lower surgically. Operating robotically is a bloodless procedure that allows doctors to save the nerves that enable men to get erections.

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Media

Jesus Angulo - Opening Remarks

Joseph Osborne - Introducing Dr. Kantoff

Philip Kantoff

Phillip Kantoff, Curtis Pettway, Brian Harper and Patrick O’Connor (Panel Discussion)
Video 1
Video 2

Congressman Charles Rangel

Curtis Pettaway

Timothy Rebbeck

Folakemi Odedina

Olorunseun Ogunwobi

Douglas Scherr

Joseph Osborne - Poster Awards Ceremony/Concluding Remarks
Biographies

Keynote Speakers

Dr. Philip Kantoff is the Chairman of Medicine at Memorial Sloan-Kettering Cancer Center. He is also the incumbent George J. Bosl Chair in Medicine. Dr. Kantoff oversees the clinical care, translational and clinical research of over 350 faculty members. He ensures the mentorship of fellows and junior faculty and cares for patients with prostate cancer. Dr. Kantoff’s laboratory-based research is devoted principally to the genetics and genetic epidemiology of prostate cancer, resistance to androgen deprivation therapy and the discovery of new biomarkers as potential prognostic and therapeutic targets. He lectures widely on both his research and the care of patients with these malignancies. Prior to his position at Memorial Sloan-Kettering, Dr. Kantoff served in multiple capacities at the Dana-Farber Cancer Institute and Harvard Medical School for over 28 years. He was Professor of Medicine at Harvard Medical School and the first incumbent of the Jerome and Nancy Kohlberg Chair in Medicine. His roles included the Director of the Lank Center for Genitourinary Oncology where he supervised the clinical care, and the clinical and fundamental research within this Disease Center, which is devoted to genitourinary malignancies. He also served as leader of the Prostate Cancer Program at the Dana-Farber/Harvard Cancer Center, and PI of the Dana-Farber/Harvard Cancer Center Prostate Cancer SPORE. He served as Vice Chair, Department of Medical Oncology and Chief, Division of the Solid Tumor Oncology, responsible for fostering the research in all of the Solid Tumor Disease Centers and ensuring the career development of its approximately 80 faculty members. Finally, he served as Chair, Executive Committee for Clinical Research.

Dr. Curtis Pettaway is Professor of Urology at The University of Texas MD Anderson Cancer Center in Houston Texas. The goal of his prostate related studies is to 1) further define host and molecular markers of cancer progression, and 2) to reduce disparities in prostate cancer outcome among African Americans and the underserved by studying both clinical and biologic correlates of aggressive disease. He is the medical director of the Prostate Outreach Project that has educated and screened over 5,000 men. He directs a National Cancer Institute funded study evaluating the influence of West African Ancestry on the incidence and aggressiveness of prostate cancer among African American and Puerto Rican populations.
Panelists:

Philip Kantoff, MD

Curtis Pettaway, MD

Reverend Patrick Hugh O’Connor is the lead pastor and chief visionary of the First Presbyterian Church in Jamaica, a multicultural, purpose driven congregation in Jamaica, Queens, New York. He has served this congregation since 1992. Reverend O’Connor received his formal education from Munro College, the University of the West Indies, the United Theological College of the West Indies, Yale University Divinity School and Columbia University. Patrick is also a graduate of the Columbia Business School, Institute for Not-for-Profit Management, Executive Level Program and the Beeson Institute for Advanced Church Leadership offered by Asbury Theological Seminary. Reverend O’Connor is passionate about community engagement and the development of people and commits himself to programs which have that vision. Patrick is married to Marcia and they have two children, Ashley and Zachary.

Dr. Brian L. Harper attended Brown University for his undergraduate education where he received a B.A. in Biology and a B.A. in Afro-American Studies. He went on to receive his medical degree from the State University of New York, Health Science Center at Syracuse, and a Masters Degree in Public Health from Columbia University. His postgraduate experience started at Harlem Hospital Center, in New York City, where he completed an internship in Internal Medicine. He continued his training at the State University of New York, Health Science Center at Stony Brook, where he completed a combined residency in General Preventive Medicine and Public Health. Dr. Harper is Board Certified in Preventive Medicine and Public Health. Dr. Harper has worked as a physician at the Rikers Island Medical Unit, served as the first Director of the Bureau of HIV Services at the Nassau County Department of Health, and as the Senior Vice President of Community Affairs at the Nassau University Medical Center. In this role, Dr. Harper served as the medical director for a network of seven community health centers where he remodeled medical services to conform to hospital standards and successfully passed two JCAHO (Joint Commission on the Accreditation of Health Care Organizations) surveys. Dr. Harper was then appointed as the first African American Commissioner of Health for Suffolk County, New York. During his tenure, he successfully managed a Department of 1500 employees with a budget of approximately $450 million. Dr. Harper also created new innovative programs including a HIV Commission and an Office of Minority Health to address health inequities. Dr. Harper then served as the Chief Operating Officer and Medical Director of the Ralph Lauren Center for Cancer Care and Prevention. This Center was a partnership between Memorial Sloan Kettering Cancer Center and North General Hospital that was initially
designed to provide quality cancer care to the residents of Harlem and surrounding areas, irrespective of a patient’s ability to pay. He is now working at the N.Y. Institute of Technology School of Osteopathic Medicine as an Associate Professor and Medical Director of the Academic Health Centers. The two health centers provide primary care and other specialty services and assist in the training of medical students in outpatient care.

**Plenary Speakers**

**Dr. Timothy Rebbeck** is Professor of Epidemiology at the Dana Farber Cancer Institute and the TH Chan School of Public Health at Harvard University. He leads molecular epidemiology studies of cancer etiology, outcomes, health disparities, and global health. He currently leads international cancer consortia that study 1) cancer in BRCA1/BRCA2 mutation carriers, and 2) prostate cancer in men of African descent in North America, the Caribbean, and Africa.

**Dr. Folakemi Odedina** is Professor in the Colleges of Pharmacy and Medicine; and Director of Diversity and Inclusion for the UF CTSI Translational Workforce Development Program. She is also the Program Director of the NIH/NCI Florida MiCART Center; Director of the Research Core for the Florida Health Equity Research Institute (HERI); PI of the NCI EGRP Prostate Cancer Transatlantic Consortium (CaPTC); and founding chair of the Florida Prostate Cancer Health Disparity group. In 2009, her leadership in health disparities was recognized by the American Society of HealthSystems Pharmacy (ASHP) and the Association of Black Health-System Pharmacists (ABHP) when she was awarded the Inaugural (1st) Leadership Award for Health Disparities. Due to her extensive experience in CaP disparity research, she was selected by the US Congressionally Directed Medical Research Programs to give the inaugural (1st) Dr. Barbara Terry-Koroma Health Disparity Legacy Lecture in 2013.

Dr. Odedina has a global consortium focused on understanding the burden of prostate cancer (CaP) disparities in Black men of West African ancestry, and developing tailored and targeted community-centered interventions to eliminate health disparities in minority populations. Her research traverses across the world with an international consortium group in the United States, Africa, Caribbean Islands, and Europe. Supported by funds from the NIH/National Cancer Institute (NCI) and Department of Defense, she is working with multiple investigators to develop a global bio-behavioral model of CaP risk factors in Black men. She has directed over 30 research projects. She is well published, has received numerous national and international awards for her work, and serves on several national and international cancer initiatives. Her landmark research on CaP disparities has been recognized by many organizations, including the American Association for Cancer Research (AACR) during the 2010 Cancer Disparities
Conference and the DOD PCRP during the 2011 Innovative Minds in Prostate Cancer Today (IMPaCT) conference. Her work has also been featured in multiple medical news including the Medscape Medical News and Oncology News. Her international accomplishments includes leading the African Cancer Control Plan published by AORTIC, contributing to the preparation of the World Cancer Report 2013 by the World Health Organization (WHO) and authoring two chapters of a Handbook for Cancer Research in Africa being published by the WHO.

Dr. Olorunseun Ogunwobi received his medical degree (MBBS) at the University of Ibadan, Nigeria. He accepted an International Student Scholarship to complete a Master’s degree in Biomedical Science at the University of Hull, United Kingdom. He subsequently accepted funding by the Norfolk and Norwich University Hospital Bicentenary Trust to complete PhD in Cancer Biology at the University of East Anglia, Norwich, United Kingdom. As a NIH-funded postdoctoral fellow at the University of Florida (UF), Dr. Ogunwobi was awarded a Master of Science degree in Clinical and Translational Science (MS-CTS) after utilizing a CTSA/NIH-funded scholarship to complete specialized training at the UF Clinical and Translational Science Institute. Dr. Ogunwobi is now Associate Professor in the Department of Biological Sciences at Hunter College. He is also a member of faculty for the PhD program in Molecular, Cellular, and Developmental Biology as well as for the PhD program in Biochemistry at the University of New York. And he is an adjunct faculty member in the Joan and Sanford I. Weill Department of Medicine, Weill Cornell Medicine, Cornell University. An active area of research in Dr. Ogunwobi’s laboratory is the role of non-coding RNAs in prostate tumorigenesis especially in Black men who are disproportionately affected.

Dr. Douglas Scherr is the Clinical Director of Urologic Oncology and Professor of Urology at the Weill Medical College of Cornell University. Dr. Scherr received his undergraduate degree in Government at Cornell University. After a year in Shenyang, China, Dr. Scherr completed his medical training at The George Washington University School of Medicine in Washington, D.C. Following this he completed a 6 year residency in Urology at The New York Hospital-Cornell University Medical Center. Subsequently, Dr. Scherr then went on to pursue a Fellowship in Urologic Oncology at Memorial Sloan Kettering Cancer Center in New York for two years. Beginning in 2001, Dr. Scherr has been on the full time faculty in the Department of Urology at Cornell where he has his current appointment. Dr. Scherr’s clinical focus is in the treatment of urologic malignancies. In particular, the treatment of prostate cancer, bladder cancer, kidney cancer and testicular cancers as well as genitourinary and retroperitoneal sarcomas. Dr. Scherr was the first physician at Cornell to perform a robotic prostatectomy and he has since performed thousands of these procedures and travels nationally and internationally teaching the procedure to many urologic surgeons. Dr. Scherr has expanded his robotic practice to now include robotic assisted removal of bladders with
total bladder reconstructions. Dr. Scherr has published extensively in the areas of bladder and prostate cancer as well a wide variety of other urologic malignancies. In addition to his clinical responsibilities, Dr. Scherr also has an active role in the Laboratory of Urologic Oncology. Dr. Scherr has been instrumental in defining the hormonal regulation of bladder cancer and is now developing a novel class of compounds that utilize the innate immune system to fight urologic tumors.