

News from The Deane Center

■ A scientific podium presentation by Dr. Natan Bar-Chama, who specializes in male sexual dysfunction at the Deane Center, and colleagues from the



Natan Bar-Chama, MD

Mount Sinai Departments of Urology and Cardiology, was selected as one of the "Best 10 Clinical Podium Talks" for the November 20th Plenary Session at the Sexual Medicine Society of North America's 15th Annual Fall Scientific Meeting. Entitled "Erectile Dysfunction is Strongly Associated with High Risk Coronary Artery Calcification in Middle-Aged Men," the presentation was based upon a study of 748 men at high risk for cardiovascular disease (CVD). The team observed a significant association of ED with coronary artery calcium scores (CACS), providing further evidence that ED serves as a marker for CVD.

■ At the same meeting, Dr. Bar-Chama presented a poster session based on a second study, this one entitled "The Use of Endo-PAT 2000® as a Marker for Endothelial Dysfunction in Patients Presenting with Erectile Dysfunction." The study utilizes an office-based diagnostic modality, the Endo-PAT 2000 manufactured by Itamar Medical, Israel, to measure endothelial dysfunction. (Endothelial cells line the interior surface of blood vessels.) The study involved 165 patients about to undergo evaluation for ED, and also included patient history, physical examination, and laboratory studies. Endothelial dysfunction was found in 33.9% of patients, and borderline endothelial dysfunction was identified in 27.3% of patients. This study further supports that erectile dysfunction is a risk factor for cardiovascular events.

■ Michael A. Diefenbach, PhD, a health psychologist with the Deane Center who is an expert on medical treatment decision making, was recently honored to be invited to attend a highly prestigious "think tank" on health care decision making, health literacy and health policy at the Max Planck



Michael A. Diefenbach, PhD

Institute in Germany as part of the Ernst Strüngmann Forum. The title of the Forum was "Better Doctors, Better Patients, Better Decisions: Envisioning Healthcare 2020." International experts ranging in expertise from medical decision making, internal medicine, epidemiology, health policy, health insurance, and the media met in small working groups over several days and ultimately produced a scholarly White Paper at the end of the session on the topic, which will be published next year as a book. The Max Planck Institute is sponsored by the German government and is renowned for bringing together experts on a wide variety of topics for the advancement of science.

■ The November 2009 issue of *Urology Times* featured an article entitled "Robot-Assisted RP: Recent Technical Modifications" based on Dr. David B.



David B. Samadi, MD

Samadi's innovative and highly successful robotic prostatectomy techniques. Regarded as a pioneer in the field of robotic surgery, Dr. Samadi is Chief, Division of Robotics and Minimally Invasive Surgery at Mount Sinai. The article presented a very detailed description of every aspect of the procedure, emphasizing nerve sparing and bladder neck reconstruction techniques, along with a series of operative photographs illustrating various stages of the operation. Noted Dr. Samadi, "These modifications are primarily designed to reduce positive surgical margin rates and improve continence and potency rates." He added, "We do not view the robot as a good unto itself, but, rather, as a tool that permits enhanced anatomic radical prostatectomy by improving vision and allowing angles of dissection not possible with open or straight laparoscopic instruments." ■

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Toxicity was limited and survival was extended on average four months. Viewed another way, at 3 years post vaccination approximately 1 in 4 men who received the placebo were alive versus 1 in 3 who received the vaccine. While this may seem like a modest effect, it should be noted that currently there is only one other FDA approved treatment for men with hormone refractory metastatic cancer; docetaxel, which improves survival by two months and has more toxicity than vaccine therapy. The Dendreon vaccine data has been submitted to the FDA, with the expectation of approval within the next six months for the treatment of advanced metastatic prostate cancer.

While the development of a dendritic cell vaccine represents a significant advance in cancer research, not just for men with prostate cancer but for the field of oncology itself, clearly this vaccine is not the panacea that many patients expected. While improvement of survival is the ultimate goal of cancer treatment, decreases in PSA or reduction in disease burden as evidenced by CT scan or bone scan in treated patients are rare events in this patient population. Many patients find it difficult to reconcile the fact that the treatment may be helping them while their PSA, which they have been hoping stays low, continues to rise.

CONTACT US If you have a comment about an article, or would like to see a particular topic featured in *The Deane Center Quarterly*, we'd love to hear from you. We welcome your feedback. Moving? Let us know your new address, so you don't miss an issue. Contact: Linda Rosenbaum, *Director, External Relations*, 212-241-0985 or linda.rosenbaum@mountsinai.org

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THE BARBARA AND MAURICE DEANE PROSTATE HEALTH AND RESEARCH CENTER

The Deane Center QUARTERLY

WINTER 2010

TODAY AT THE DEANE CENTER

Vaccine Therapy for Prostate Cancer: Is It Ready for Primetime?



Simon J. Hall, MD

Harnessing a patient's own immune system to target cancer cells has long been a goal of many medical researchers, who view this approach as a potentially non-toxic, natural cancer therapy. As I write this column, we may in fact be approaching the dawn of a new era for cancer patients...marshalling the body's own defense system to destroy cancer cells.

As previously noted in the *Deane Center Quarterly*, Dendreon, a Seattle-based biotechnology company, has developed a product called Sipuleucel-T, a vaccine made from individual patients' own dendritic cells. Found in blood, skin and the lining of the intestines, dendritic cells recognize and process foreign substances and can initiate an immune response.

To treat prostate cancer, these cells are removed from the patient and in cell culture are exposed to prostatic acid phosphatase, a protein only made by prostate cancer cells. The dendritic cells internalize this protein and become activated against it. The cells are then infused back into the patient, a process that is repeated twice to complete a course of treatment. The activated dendritic cells initiate a T-cell response to target and kill cells that express prostatic acid phosphatase in the body. To date, more than 600 men with advanced prostate cancer, including patients at the Deane Center, have received the vaccine in Phase III clinical trials.

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MOUNT SINAI SCHOOL OF MEDICINE

Leading Prostate Cancer Clinician & Scientist William K. Oh, MD, to Collaborate with Deane Center Physicians at Mount Sinai

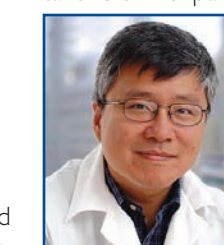
Dr. Oh is Named Chief of the Mount Sinai Division of Hematology and Medical Oncology, Co-Director of the Prostate Cancer Program and Associate Director for Clinical Research at The Tisch Cancer Institute.

Mount Sinai's recent recruitment of internationally renowned researcher and clinician William K. Oh, MD, represents a major opportunity to advance the institution's reputation in the area of genitourinary (GU) malignancies, including prostate, renal, bladder and testicular cancers. Dr. Oh comes to Mount Sinai from the Dana-Farber Cancer Institute in Boston, where he was Clinical Director of the Lank Center for Genitourinary Oncology and directed the Gelb Center for Translational Research. At Dana-Farber, he developed a clinical database and specimen repository for GU cancers that included samples from more than 8,000 patients, which yielded significant data about the development and treatment of prostate, renal and bladder cancers.

Dr. Oh has been named Chief of the Division of Hematology and Medical Oncology, Co-Director of the Prostate Cancer Program and Associate Director for Clinical Research at The Tisch Cancer Institute. Dr. Oh will also serve as Professor of Medicine and Urology, and the Ezra M. Greenspan, MD, Professor in Clinical Cancer Therapeutics at Mount Sinai School of Medicine.

Acceleration of Prostate Cancer Research and Expansion of Multidisciplinary Prostate Program Planned

As Co-Director of the Prostate Cancer Program, Dr. Oh will be collaborating with Simon J. Hall, MD, Chairman of the Department of Urology and Director of The Barbara and Maurice Deane Prostate Health and Research Center, and other members of the Deane Center faculty on several exciting research projects relating to prostate cancer. He will also play an important role in expanding the multidisciplinary prostate



William K. Oh, MD

cancer program at the Deane Center. "As a highly respected researcher and clinician, Dr. William Oh will be a major asset to the Deane Center," says Dr. Hall. "His efforts to further the understanding of the molecular aspects of cancer will have an

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William K. Oh, MD Teams with Deane Center

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impact on the development of future prostate cancer treatments. In addition, his experience creating tumor banks and utilizing bioinformatics to understand the genetics of cancer will further serve to enhance our knowledge base. All of us associated with the Deane Center are very excited to welcome Dr. Oh to Mount Sinai."

Promising Trials Targeting Men with High Risk, Localized Prostate Cancer

One of Dr. Oh's primary research interests is treating men with high risk, localized prostate cancer. He has conducted three clinical trials targeting men with the highest chance of relapse by using chemotherapy and novel agents in a neo-adjuvant setting. This involves a systemic approach with drug therapy prior to treatment, either surgery or radiation. According to Dr. Oh, approximately 20–30% of men in the United States fit the diagnosis of high risk upon diagnosis. Many of these high risk men are likely to have cancer that has already escaped the prostate. "The Phase II study that I recently completed at Dana-Farber in collaboration with Duke University combined Taxotere, a chemotherapeutic agent, with a drug called Avastin, which blocks the tumor blood supply," Dr. Oh explains. "Candidates for the trial had to have "high risk" cancer, for instance with a Gleason score of 8, 9 or 10, evidence on an MRI of cancer that was breaking out of the prostate, or a PSA over 20 ng/ml.

"The regimen was very well tolerated and we saw some very interesting results, particularly demonstrating that Avastin enhanced the effect of the Taxotere in terms of degree of shrinkage of the tumor," Dr. Oh continues. "We are very encouraged by these results to date and believe this approach has the potential to maximize the benefits of surgery and prevent a recurrence. We're now in the early stages of designing the next phase of the study, which will take place at Mount Sinai. This is a very important area of research in prostate cancer, because these are the men most at risk of relapsing and dying from their disease. The hope is that this approach will cure these men."

Asking Questions, Finding Answers: Collecting Blood, DNA, Tissue Samples

Dr. Oh is also in the process of creating a prostate cancer database and repository of blood, DNA and tissue samples at Mount Sinai. "A large, very robust database such as we envision creating at Mount Sinai will allow us to ask many questions about our prostate cancer patients and their disease... who got cancer, why they got cancer, the underlying genetics of

the cancer," says Dr. Oh. "We then will divide the patients into sub-groups of slow growing and fast growing cancers and will be able to look at molecular predictors of disease progression."

Dr. Oh makes the very important point that patients participating in the database project need not worry about privacy and potential insurance issues. "All we require from patients is their written permission to store their samples and follow their clinical data, permission to collect blood at least once in the majority of patients, and permission to collect any prostate tissue not needed by the pathologist, which would otherwise be discarded. Ultimately, none of the data will be associated with specific patients, insuring that privacy issues are respected. The goal is to pool all the data to understand the biology of prostate cancer, not to link any of this information to an individual, a fact which will be reflected in the consent form."

Decoding the Genetics of Prostate Cancer to Simplify Diagnosis

Dr. Oh is also working on the development of a six-gene signature to predict prostate cancer via a blood test, that when combined with the PSA level is a much more accurate diagnostic tool. "In our preliminary studies, the accuracy of this combination approach was in the 95% range at predicting the men who had prostate cancer," notes Dr. Oh. "We're very encouraged by these early results. We're now opening a national multi-center study called PRECISE. At Mount Sinai, Dr. Hall will be the lead investigator, while I will oversee the national program.

"Our goal is to eventually validate that this six-gene signature is better than PSA alone at predicting a positive prostate biopsy. We know that if a man has an abnormal PSA, he is told that his chance of having a positive biopsy is about 33%. ...which means 1 out of 3 men going in for a prostate biopsy will have prostate cancer but 2 out of 3 will not have prostate cancer and will have to undergo a painful, unpleasant biopsy. Ultimately, by more accurately predicting whether or not a man has prostate cancer with just a simple blood test, we will be able to eliminate the need for thousands of unnecessary prostate biopsies each year."

Dr. Oh has authored more than 150 original articles, reviews and book chapters and has recently edited two books on prostate cancer. He is on the editorial boards of *Clinical Genitourinary Cancer* and the *American Journal of Hematology and Oncology*. A native New Yorker, Dr. Oh earned his medical degree from New York University. He completed his residency in internal medicine at Brigham and Women's Hospital in Boston and subsequently completed a fellowship in medical oncology at the Dana-Farber Cancer Institute. ■

Active Surveillance is a Viable Alternative for Men with Limited Amount of Low-Grade Prostate Cancer

"Pathologically, up to 20% of men undergoing radical prostatectomy are found to have insignificant disease, indicating that this group of patients might have been treated prematurely."

With the recent controversy swirling around the topic of the value of PSA testing and the over-diagnosis and over-treatment of prostate cancer, an approach referred to as active surveillance now more than ever is of interest, both to urologists in practice and newly diagnosed patients. "Active surveillance" refers to an alternative to definitive treatment with surgery or radiation for patients diagnosed with a small volume of low-grade (as determined by Gleason score) prostate cancer, identical to what are found at autopsy of men; approximately 30% of 50 year olds and approximately 75% of 70 year olds.

The use of the term active surveillance was designed to underscore the fact that any sign of disease progression would initiate treatment with the goal of curing the cancer; this is a different approach from an earlier option, watchful waiting, where there was never an intention to definitively treat the patient if the disease progressed. Active surveillance involves very close monitoring, typically quarterly physical examinations by a urologist and PSA testing, as well as prostate biopsies every 12 to 18 months, regardless of whether changes are discovered in PSA or physical examination.

At the Deane Center, Dr. Hall and behavioral health psychologist Michael A. Diefenbach, PhD, are currently engaged in an ongoing study of patients on an active surveillance protocol. "During the past decade, the widespread use of PSA screening has led to an increase in the diagnosis of prostate cancer and an increase in the detection of lower risk cancers, which has resulted in an increase in treatment, such as radical prostatectomy," notes Dr. Hall. "Pathologically, up to 20% of men undergoing radical prostatectomy are found to have insignificant disease, indicating that this group of patients might have been treated prematurely. Active surveillance is an attempt to find these patients prior to definitive treatment."

There was also considerable media interest at the most recent annual meeting of the American Urological Association, where a group of researchers from Toronto presented an abstract based on a study of 453 patients enrolled in an active surveillance program who have been followed on average for 7

"Our ongoing study is designed to demonstrate that active surveillance is a viable option for a very specific sub-set of men with minimal, low-grade disease."

years. Thirty-five percent ultimately were reclassified as higher risk and offered definitive therapy.

The Epstein criteria is one of the most widely followed for selecting patients for active surveillance protocols, restricting enrollment of men with non-palpable prostate cancers who have Gleason scores no greater than 4 or 5, no more than 2 positive cores, and no more than 50% of any single core involved with cancer. Several published reports have indicated that with these criteria approximately 30% of patients go on to treatment within 3 years due to progression of disease. The Mount Sinai active surveillance study has even more stringent entry criteria, allowing only men with one positive core with 10% or less cancer. Entry into the protocol is dependent on a confirmatory biopsy, usually 3 months after the first biopsy, to exclude those patients with a higher volume or grade cancer that was missed on the first biopsy. Patients also have their PSA levels measured every 3 months and receive a digital rectal exam every 6 months and surveillance biopsies every 18–24 months, or earlier based on rising PSA or patient request. Recommendations for therapy are based on disease progression as represented by an increase in number of positive cores or Gleason score on biopsy, PSA velocity and PSA doubling time while on surveillance have not been predictive of disease progression.

According to Dr. Hall, "Our ongoing study is designed to demonstrate that active surveillance is a viable option for a very specific sub-set of men with minimal, low-grade disease. Patients with multiple cores of low grade cancer or higher grade cancer are urged to undergo treatment. The term active surveillance suggests a very proactive approach to monitoring for disease progression in these low risk men so that we can offer treatment with surgery and radiation if necessary at a time when active intervention has the greatest potential to be curative. To date, we have seen a very low rate to progression with our specific criteria."

Dr. Hall and Dr. Diefenbach have applied for a federal research grant to expand the scope of the study to include a detailed psychological questionnaire, analyzing levels of stress in men on surveillance versus those who decide on treatment. Says Dr. Diefenbach, "The feelings of ambiguity that are often associated with not taking a more definitive approach to treatment with surgery or radiation, as well as the stress related to this uncertainty, can become a barrier to choosing active surveillance. This study is designed prospectively to ascertain the levels and sources of stress in men who are under surveillance versus those who are treated." ■

Simon J. Hall, MD, Named Kyung Hyun Kim, MD Chair in Urology at 2009 Mount Sinai Convocation



Marking the occasion, Dr. Kenneth L. Davis, President and Chief Executive Officer, Mount Sinai Medical Center, presents Dr. Simon J. Hall with a commemorative plaque officially naming him the first Kyung Hyun Kim, MD Chair in Urology.

Leo C. Stern Auditorium in The Annenberg Building on Tuesday, September 22nd, Dr. Simon J. Hall, MD, was named the first Kyung Hyun Kim, MD Chair in Urology.

The endowed chair was established through a generous gift from Mrs. Ae Rim Kim in honor of her late husband Kyung Hyun Kim, MD, who practiced urology in Ohio prior to his death in 2004. He attended the College of Medicine at Kyungpook



Department of Urology colleagues (left to right) Dr. Courtney K. Phillips, Michael A. Diefenbach, PhD, Dr. Jeffrey A. Stock, Dr. Natan Bar-Chama and David B. Samadi flank honoree Dr. Simon J. Hall.

National University in Daegu, South Korea, where he earned his MD in 1964. He interned at Misericordia Hospital in the Bronx and was a resident in general surgery at Mount Sinai Hospital from 1966 to 1967 prior to beginning his urology residency at Mount Sinai, which he completed in

1971. He remained a member of the faculty until he relocated his family to Ohio in 1973. Dr. Simon J. Hall, who in addition to serving as Urology Chair, is Director of The Barbara and Maurice Deane Prostate Health and Research Center and Co-Director with Dr. William K. Oh of the Mount Sinai Prostate Program. He has been widely praised as an award-winning clinician, educator and researcher. Dr. Hall's research has focused on many aspects of prostate cancer, from preclinical studies of gene therapy approaches to treating metastatic prostate cancer, to clinical trials of a vaccine therapy for advanced prostate cancer. Dr. Hall currently holds the position of Chairman, GU Section of the Cancer Center's Protocol Review and Monitoring Committee and is President of the Executive Committee of the New York Academy of Medicine's Section of Urology. He earned his medical degree from Columbia University's College of Physician and Surgeons. Dr. Hall served his internship and junior residency at Mount Sinai, prior to becoming a resident and then Chief Resident in Urology at Boston University's Department of Urology. He also served as a uro-oncology fellow at Baylor College of Medicine.

Mrs. Kim, who traveled to New York from her home in Lakeland, Florida for the ceremony, looked on proudly, along with her sons, William Y. Kim, MD, an oncologist in practice in Chapel Hill, North Carolina, and James Y. Kim, MD, an internist in Greensboro, North Carolina, during the procession of honorees and when Dr. Kenneth L. Davis, President and Chief Executive Officer, Mount Sinai Medical Center, presented Dr. Hall with a commemorative plaque officially naming him the Kyung Hyun Kim, MD Chair in Urology. Along with congratulate Dr. Hall, all suitably outfitted in academic robes, were members of the Department of Urology Faculty. ■

UPCOMING COMMUNITY EVENTS

MAN TO MAN

Prostate Cancer Education and Support Meetings For Survivors and Families

Wednesday, January 13, 6–8 pm

Speaker: Simon J. Hall, MD Chair, Department of Urology, Mount Sinai

Topic: Immunotherapy for Prostate Cancer: Is it Ready for Primetime?

Wednesday, March 10, 6–8 pm

Speaker: William K. Oh, MD Chief, Division of Hematology and Medical Oncology, Mount Sinai

Topic: New Treatments for Advanced Prostate Cancer

Wednesday, May 12, 6–8 pm

Speaker: Neil H. Grafstein, MD Director of Reconstructive Urology, Female Urology and Voiding Dysfunction

Topic: Minimally Invasive Strategies to Improve Urinary Control after Prostate Cancer Surgery

For more information call:

Alison Snow, LCSW/Mount Sinai Rutenberg Treatment Center 212-241-7805 or David Pulli, LMSW/American Cancer Society 212-237-3843

Man to Man meetings take place at Mount Sinai School of Medicine, 1468 Madison Avenue, Hatch Auditorium, Guggenheim Pavillion, 2nd fl.

USTOO

Thursday, January 21, 6–8 pm

Speaker: Simon J. Hall, MD Chair, Department of Urology, Mount Sinai

Topic: Immunotherapy for Prostate Cancer/Clinical Trials 101, New York Presbyterian/Weill Cornell Medical Center, 1300 York Avenue at 69th Street, Room A126