Pelican/Peter Michael Bi-Annual Prostate Cancer Colloquium

New York University Langone Medical Center

October 25 & 26, 2012

See page 7 for a list of all attendees

International Collaboration

The Pelican Cancer Foundation (UK) and the Peter Michael Foundation (US) co-sponsored and co-hosted an international colloquium on the MRI-Guided Prostate Biopsies in Prostate Cancer. US studies have found that targeted prostate biopsy with magnetic resonance imaging (MRI) significantly increased the rate of cancer detection. The goal of the Pelican/Peter Michael Colloquium was to help develop formal standards for the use and reporting of MRI-guided prostate biopsies. This was an active working conference attended by urologists, radiologists and methodologists from Europe, North America and Asia. Their collaboration resulted in an important consensus paper which has been published in *European Urology*. The paper's Abstract is presented below.

Standards of reporting for MRI-targeted prostate biopsies (START): recommendations from an international working group

Background

A systematic literature review of MRI-targeted prostate biopsy demonstrates poor adherence to the Standards for Reporting of Digagnostic studies (STARD) recommendations for the full and transparent reporting of diagnostic studies.

Objective

To define and recommend STAndards of Reporting for mri-Targeted biopsy studies (START).

Design, setting and participants

A panel of 23 experts in urology, radiology, histopathology and methodology used RAND/UCLA appropriateness methodology. A 258 statement pre-meeting questionnaire was scored by each panelist. The collated responses were presented at a face-to-face meeting and each statement was rescored after group discussion.

Outcome measurements and statistical analysis

Measures of agreement and consensus were calculated for each statement. The most important statements, based on group median score, the degree of group consensus and the content of the group discussion, were used to create a checklist of reporting criteria (the START checklist).

Results and Limitations

The strongest recommendations were to report histological results of standard and targeted cores separately using Gleason score and maximum cancer core length. A table comparing detection rates of clinically significant and clinically insignificant disease by targeted and standard approaches should also be used. It was recommended to report the recruitment criteria for MRI-targeted biopsy, prior biopsy status of the population, a brief description of the MRI sequences, MRI reporting method, radiologist experience, and image registration technique. There was uncertainty about what histological criteria constitutes clinically significant cancer when the prostate is sampled using MRI-targeted biopsy and it was agreed that a new definition of clinical significance in this setting will need to be derived in future studies.

Conclusions

Use of the START checklist would improve the quality of reporting in MRI-targeted biopsy studies and facilitate a comparison between standard and MRI-targeted approaches.

Imaging of PSMA in Prostate Cancer and Beyond

Please note that all text under *Original Proposal* is a significantly reduced from the four to six page proposals submitted by the institutions. Please contact the Foundation if you would like to read the original full research proposals.

Memorial Sloan-Kettering Cancer Center

Principal Investigator:

Hedvig Hricak, MD, PhD, DrHC

Chairman of Department of Radiology
Carroll and Milton Petrie Chair

Peter Michael Postdoctoral Fellow:

Hebert Alberto Vargas, MD, MS

Original Proposal

The overall goal of the project is to develop new tools to detect prostate cancer. Using the same imaging agent, we aim to furthermore detect cancer independent of the tumor type by their neovasculature. The objective of this proposal is to gain insights into the function of prostate specific membrane antigen (PSMA) in prostate cancer and tumor neovascularization utilizing novel imaging probes and to exploit these to monitor current and create future therapies. PSMA can provide several valuable advantages over other antigens, because i) the expression on prostate cancer and neovasculature of other tumors (and lack thereof on normal vasculature) makes it an ideal tumor target; ii) dose-dependent internalization of PSMA results in accumulation of the targeted agent in the tumor; and iii) the enzymatic activity can be used to image PSMA function with an activatable probe and to treat tumors with a prodrug.

Progress Report

Dr. Olivio Donati

Dr. Omer Aras

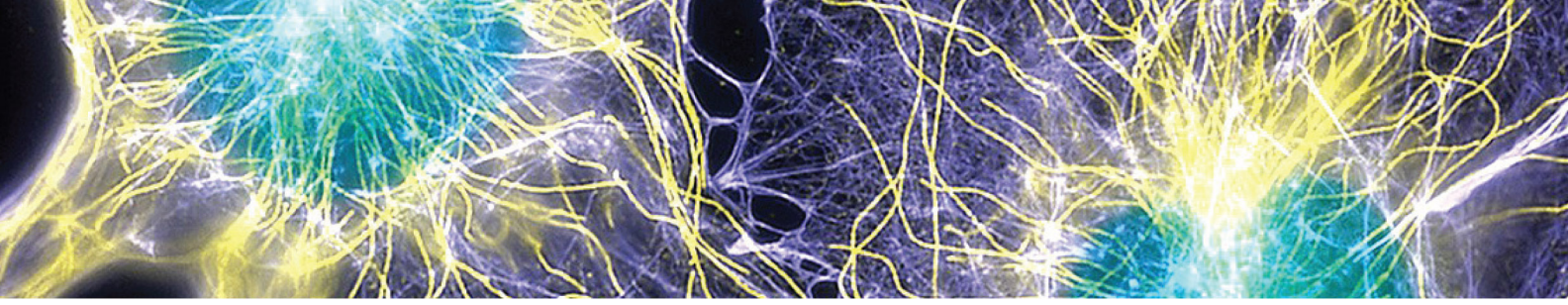
This year, the Peter Michael Fellowship supported the work of three budding academic stars at Memorial Sloan-Kettering Cancer Center (MSKCC): Dr. Hebert Alberto Vargas, who is now a junior faculty member in our Department of Radiology; Dr. Olivio F. Donati, a visiting radiology research fellow from Switzerland, who will join the faculty of the University Hospital, Zurich in May and will specialize in prostate imaging; and Dr. Omer Aras, who arrived from the National Cancer Institute with a strong background in basic science, a patent related to stem cell imaging, and a desire to expand his expertise to the field of prostate cancer imaging. These three investigators have been working closely with other members of the prostate cancer management team to investigate the value of conventional and molecular imaging techniques for improving prostate cancer care. Their projects are summarized below.

MRI for pretreatment assessment of clinically low-risk prostate cancer

This year, two studies described in last year's report concerning the detection and characterization of clinically low-risk prostate cancer by MRI were published in the leading imaging and urology journals, *Radiology* and the *Journal of Urology*. Dr. Vargas was the first author of both manuscripts (1-2). *See page 7, column 2 for publications list.*

DW-MRI of the prostate: application in the transition zone

Generally, the value of DW-MRI for detecting prostate cancer in the transition zone of the prostate has been deemed limited due to the confounding effects of benign prostatic hyperplasia (BPH). However, most publications on diffusion-weighted MRI (DW-MRI) of the prostate have focused only on the peripheral zone of the gland. Drs. Donati and Vargas participated in a study that examined the value of DWI for detecting cancer specifically in the transition zone (TZ). In addition to assessing the incremental value of DW-MRI to conventional MRI in



detecting TZ prostate cancer, they evaluated the correlation between DW-MRI data and TZ tumor aggressiveness and compared DW-MRI data in TZ cancer and BPH. Contrary to conventional wisdom, the findings suggested that DWI has value for both tumor detection and assessment of aggressiveness in the TZ. The study has been accepted for publication by *Radiology* (3).

Streamlining MRI exams for patients with locally recurrent prostate cancer

Efficient use of imaging technology is critical to reduce healthcare costs. Although numerous centers now perform "multiparametric MRI" exams of the prostate that combine conventional anatomic MRI with both dynamic contrast-enhanced (DCE) and diffusion-weighted (DW) MRI, for many applications, the need to include all three types of MRI has not been demonstrated. Drs. Donati and Vargas conducted a study examining which sequences are truly necessary for detecting locally recurrent prostate cancer after radiotherapy. They found that while the combination of conventional MRI and one or more functional imaging techniques always yielded greater accuracy than MRI alone, the optimal approach was to combine conventional MRI only with DW-MRI, as DCE-MRI did not add significant value to the other two sequences. The study has been accepted for publication by *Radiology* (4).

Using MRI to assess radiation-induced changes in the pelvis

For patients with local recurrence of prostate cancer after radiation therapy (RT), salvage radical prostatectomy is now recognized as the only local treatment option that can provide long-term cancer control. However, salvage radical prostatectomy is considered technically more challenging than standard radical prostatectomy and is associated with higher rates of complications. Although these high complication rates are thought to be due to radiation-induced changes in the pelvis, no detailed imaging studies have been done to confirm this theory. In a recent study, Drs. Donati and Vargas analyzed radiation-induced changes in the MRI appearances of the urethra and periprostatic tissues. The study showed differences in the changes induced by different types of RT and laid the foundation for further research, which will evaluate associations between the extent of radiation induced-changes detected on MRI and clinical outcomes, including recovery of urinary continence. Ultimately, the ability to assess radiation-induced tissue damage by MRI could aid patient selection as well as surgical planning for salvage radical prostatectomy; furthermore, when salvage prostatectomy is not an option, it could help determine whether the patient can tolerate additional radiation. This study is being submitted to the *International Journal of Radiation Oncology, Biology, Physics* (5).

Identification of new prognostic biomarkers on CT and PET

Novel targeted therapies directed against the androgen receptor have shown clear survival benefits in patients with castrate-resistant metastatic prostate cancer. There is a pressing need for imaging biomarkers that can reliably monitor treatment response to these novel therapies, particularly in bone metastases, which are the leading cause of morbidity and mortality in men with advanced disease. Although CT is not considered optimal for evaluating bone metastases, it is widely available and commonly used for assessing lymph nodes and distant metastases in advanced prostate cancer. Thus, an understanding of the relationships between CT features and molecular events in the tumor microenvironment could be used to extract additional, useful information from CT exams. Dr. Vargas participated in a highly original, prospective study of patients with metastatic prostate cancer that compared CT findings to findings from molecular imaging with fluorodeoxyglucose (FDG) and the novel tracer 18F-16b-fluoro-5-dihydrotestosterone (FDHT), which identifies androgen receptors. The study found that patterns of bone lesion morphology on CT were indeed associated with molecular events seen on PET; furthermore, it showed that imaging features such as CT lesion morphology, total number of bone lesions on CT or PET, and the degree of FDHT uptake on PET were significantly associated with patient survival. The study will soon be submitted for publication, with Dr. Vargas as the first author (6).

Improving the measurement of tumor aggressiveness by DW-MRI

DW-MRI data is typically used to calculate the apparent diffusion coefficient, a metric that tends to be lower in prostate cancer than in healthy prostatic tissue. In various studies, ADC values have been found to correlate inversely with prostate tumor aggressiveness. However, because the ADC values in tumors of different Gleason grades overlap, it is not yet possible to distinguish specific Gleason grades using DW-MRI. Dr. Donati is conducting a study to assess new approaches for measuring ADC values that are designed to minimize this overlap.

Using tumor volume and ADC values to predict tumor aggressiveness by DW-MRI

In patients with prostate cancer, tumor volume is an important prognostic factor that has been shown to correlate with tumor aggressiveness. Dr. Donati is involved in a study examining whether it is possible to combine ADC values and tumor volume measurements from DW-MRI to distinguish low-risk from medium- or high-risk cancers.

Prostate Cancer: The Challenge in Detection

STANFORD
SCHOOL OF MEDICINE
Stanford University Medical Center

Principal Investigator:

Sanjiv Sam Gambhir, MD, PhD
Chairman, Department of Radiology
Director of Molecular Imaging Program
Director of Canary Center at Stanford for Cancer Early Detection
Nuclear Medicine Professor in Departments of Radiology & Bioengineering

Peter Michael Postdoctoral Fellow:

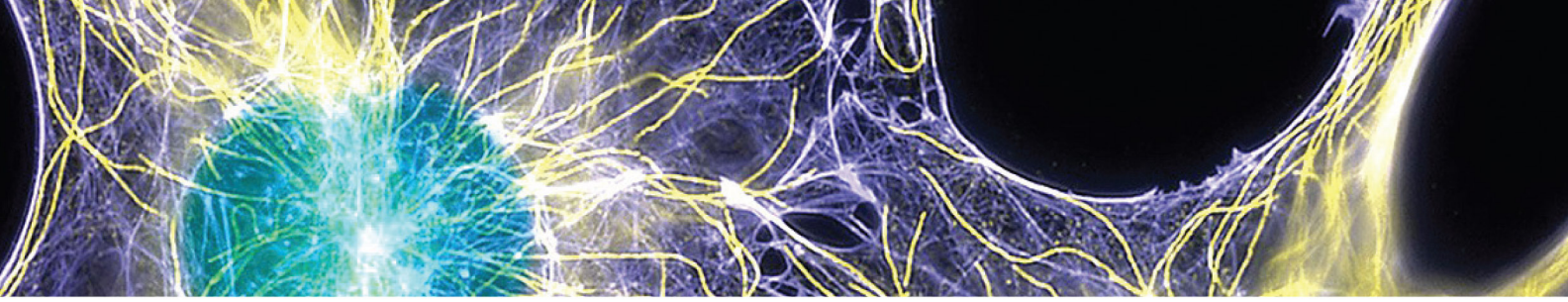
Sri-Rajasekhar Kothapalli, PhD, MS, MTech, MSc

Original Proposal

We intend to revolutionize prostate cancer management based on Theranostics – the combination and consequent synergy of state-of-the-art, multimodality molecular imaging for diagnosis with high specificity molecular-targeted therapeutics. Photoacoustic molecular imaging is an emerging technology that overcomes, to a great extent, the spatial resolution and depth limitations of whole-body optical imaging. Photoacoustic imaging is capable of monitoring molecular levels of cancer-specific proteins in a living subject. In this technique, a conventional photoacoustic imaging instrument is coupled with an imaging agent (contrast agent) targeted to a cancer-specific protein to achieve a specific imaging signal. The concept is that light goes into the body and sound comes out. Nanoengineering is employed to develop the imaging agent-- nanoparticles specifically designed to seek and identify prostate cancer at the cellular level. The imaging agent is introduced into the body and the nanotubes attach to prostate cancer cells wherever they may be, in the gland or out if the cancer has metastasized. The laser light is passed over the subject causing the nanotubes to emit an ultrasound that is captured and imaged outside of the body. The next step would be to design the nanotubes to carry a pay load. Then an audio sound could be sent back into the body that triggers the nanotubes to destroy the cancerous cells only.

Progress Report

A. Progress on Dual Modality Transrectal Ultrasound and Photoacoustic Imaging of Prostate: In years 1 and 2 of the fellowship award we used 16x16 element two dimensional (2D) Capacitive Micromachined Ultrasound Transducer (CMUT) arrays to develop a transrectal photoacoustic (TRPA) device, data acquisition (DAQ) hardware, and image reconstruction software. These components were integrated to our bench-top photoacoustic laser (Continuum Surelite III) to form a complete TRPA imaging system. Encouraged by the TRPA results in prostate tissue mimicking phantoms, in year 3 (2012) of the award we developed a dual modality transrectal ultrasound and photoacoustic (TRUSPA) imaging system for visualizing both prostatic anatomy in ultrasound mode and optical contrast of the prostate in photoacoustic mode. The DAQ hardware and software was also updated in year 3 to accommodate dual modality real time three dimensional (3D) ultrasound and photoacoustic imaging. The TRUSPA device performance was tested using surgically removed whole human prostate (n=2 prostates) obtained from two patients undergoing robotic prostatectomy at VA hospital in Palo Alto. These pilot experiments demonstrated that the TRUSPA instrument was capable of obtaining clinical grade prostatic anatomy in ultrasound mode and photoacoustic imaging depth of about 2 cm in human prostates using tubes filled with blood placed at various depths inside prostate to mimic blood vessels. In the 2nd prostate experiment with



TRUSPA, significant photoacoustic contrast was observed in the left lobe of the prostate, correlating with urologist identification of the cancerous region. More systematic studies are currently being conducted to understand the photoacoustic signatures of prostate cancer in correlation with histopathology studies.

B. Studies in Mice Prostate Cancer models and Single Cells: During the fellowship period, besides building a TRUSPA imaging device, we also investigated photoacoustic signatures of prostate cancer in mice models. Since prostate cancer is slow-growing in most cases and its management is associated with wide treatment options including active surveillance, a better imaging technique that performs diagnosis as well as predicts prognosis can help reduce the number of random biopsies, help with treatment/management selections at the right time, administer focal therapy and monitor treatment. Therefore novel imaging strategies are needed to visualize hallmarks of prostate cancer with high sensitivity and specificity. For example, a recent study on histopathology specimens of a large cohort of patients demonstrated that prostate tumors exhibit angiogenesis, a well known hall mark of cancer, and aggressive tumors tend to have blood vessels that are small, irregular, and primitive in cross-section, while indolent tumors have normal blood vessels [*Mucci LA et al., Journal of Clinical Oncology. 2009; 27(33):5627–5633*]. However, to date, no imaging modality has been reported to clearly visualize, in vivo, angiogenesis accompanying prostate tumor growth in their natural state without using any exogenous contrast agents and window-chamber models. In year 3 (2012) of the fellowship award, I have demonstrated that photoacoustic imaging (PAI) can reliably image angiogenesis in sub-cutaneous mice prostate cancer (MPC) models using intrinsic optical absorption of hemoglobin present in highly vascularized prostate tumors. These results show that PAI can monitor changes in vascularization that accompany tumor formation and growth. Further, intravenously administered FDA approved optical contrast agent, indocyanine green (ICG), improved image contrast to ~ 40 fold, inferring utility of contrast agents to visualize deep tumors. While angiogenesis is an essential hallmark of cancer, including prostate cancer, and can be readily imaged in clinic with optimized TRUSPA device, it may not help fully understand the diagnostic and prognostic features of the cancer. Therefore, we are also currently investigating biomarker-specific molecular targeting of prostate cancer, leveraging our recent advances in PA molecular imaging agents [*Levi J et al, Clinical Cancer Research 2013*]. These experiments in mice models will help achieve image metrics that can be integrated into TRUSPA device to achieve a clinical grade device that reliably visualize diagnostic and prognostic features of the cancer.

We also developed a novel real-time bio-sensing tool to identify specific proteins within the prostate cancer cells, which has applications in elucidating whether certain drug produces or inhibits a specific protein [*Shambat G, Single-cell photonic nanocavity probes, Nano Letters*].

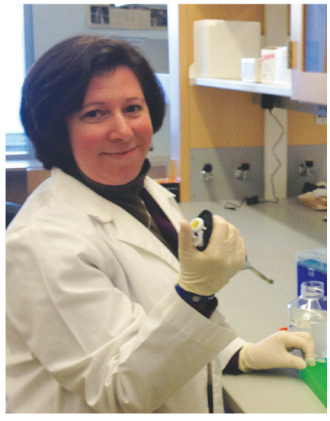
C. Future Directions in Clinical TRUSPA: (1): We recently purchased a new portable and compact photoacoustic laser (unlike the current bench-top laser) for conducting clinical trials. We are currently combining the previously discussed TRUSPA device and related DAQ with this laser system so that total experimental system can be made compact, and portable for use in and outside the surgery room in the hospital. **(2):** We will begin clinical trials with the clinical 2D-TRUSPA starting April 2013. **(3):** While two dimensional (2D) ultrasound arrays are attractive for real time three dimensional (3D) TRUSPA imaging, 1D linear ultrasound arrays, with two dimensional cross-sectional (B-mode) imaging capabilities, are used in clinical TRUS. Therefore to gain easy urologist acceptance and clinical translation, we are currently building TRUSPA device using 1D linear CMUT arrays. This 1D-TRUSPA development will be conducted by the end of March 2013. **(4):** In April 2013, the potential of 1D TRUSPA to contribute to improved TRUSPA performance will be evaluated using surgically removed human prostates and prostate mimicking phantoms. **(5):** We will follow steps mentioned in (1), to evaluate 1D-TRUSPA performance in the clinic. **(6):** We will analyze the clinical impact of 1D and 2D CMUT array based TRUSPA approaches. The approach that is expected to provide the best TRUSPA performance in humans will be used for a larger set of clinical trials starting in May/June 2013.

Stanford University Medical Center

Cell-specific Interference Strategies for Prostate Cancer

Duke Cancer Institute

UNC ESHELMAN SCHOOL OF PHARMACY



Principal Investigators:
Daniel George, MD, Duke

Rudy Juliano, PhD, UNC

Bruce Sullenger, PhD, Duke

Peter Michael Postdoctoral Fellow:
Jennifer Freedman, PhD, Duke

Original Proposal

Interference RNA (RNAi) strategies represent a potentially new targeted approach to silencing specific genetic pathways within cancer however, efficient delivery of small interfering RNA (siRNA) molecules into target cells is a major obstacle to developing this modality into effective therapy. RNA aptamers represent another novel form of RNA therapeutic – one which binds specifically to unique peptide sequences. Using an RNA aptamer for prostate specific membrane antigen (PSMA), we have created a delivery mechanism that not only results in cell specific binding, but also rapid and efficient endocytosis.

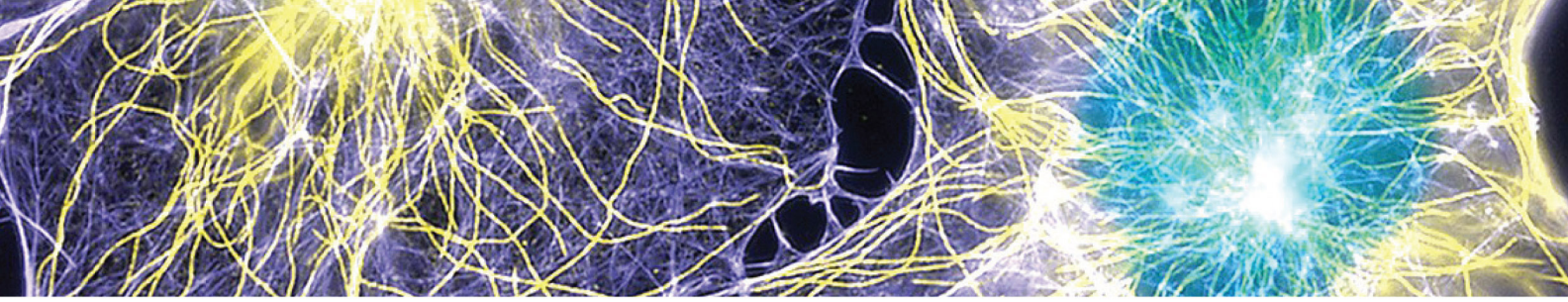
Therefore we propose to develop a novel RNA chimera, combining our PSMA aptamer with an AR-specific siRNA. We hypothesize that a PSMA aptamer-AR (androgen receptor) siRNA chimera will demonstrate cell-specific inhibition of AR that is more potent than known AR antagonists. The specific aims of the research are to:
Create and demonstrate the in vitro specificity and efficacy of the PSMA aptamer-AR siRNA Chimera. Demonstrate in vivo activity of the PSMA aptamer-AR siRNA Chimera.

Progress Report

Development of new treatments for advanced prostate cancer have significantly improved the lives of patients; and energized hope for greater progress. Drugs that block testosterone and its pro-cancer effects have significantly improved the survival of patients with prostate cancer that is resistant to other hormone therapy. However, cancer still finds a way around this treatment. Clearly, we need new treatments to block this pathway or its effects more completely.

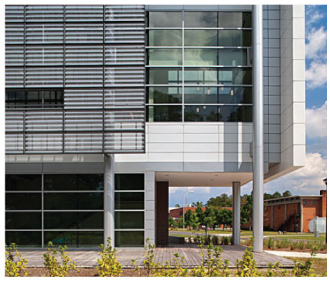
RNA is a key molecule in the biology of all cells, translating genes (DNA), into proteins. However, this critical intermediate step is frequently manipulated in cancer to alter proteins and create growth and survival signals. Recent developments suggest these alternative RNA forms could be targets for therapy or even manipulated to block the activity of pro-cancer genes.

We have leveraged our support from the Peter Michael Foundation to bring together a team of experts at Duke University Medical Center and the University of North Carolina to create a critical mass



of research in the field of RNA therapeutics focused on prostate cancer. Specifically, we have designed and synthesized a splice-switching oligonucleotide (SSO), which is a small nucleic acid that can produce a novel variant of a gene, to drive production of a protein that will block testosterone signaling. If successful this SSO product should prevent the activation of genes required for prostate cancer growth and survival. Initial results have demonstrated that when this SSO is applied to prostate cancer cells it creates a protein product that blocks a testosterone regulated target gene. Importantly, this SSO product also inactivates the pre-existing testosterone pathway present in prostate cancer cells. Our current studies are focusing on demonstrating that the SSO product is able to block additional testosterone regulated genes and inhibit the growth of prostate cancer cells. Future studies will focus on using an innovative strategy to selectively deliver this SSO product to prostate cancer cells and localize it to the compartment within the cancer cells where such a product will have a biologic effect, the cancer cell nucleus. Ultimately, this approach could add to current treatment strategies, enabling a complete inhibition of testosterone signaling in prostate cancer.

Our translational research team includes Dr. Dan George, MD, Director of Genitourinary Oncology at the Duke Cancer Institute, Dr. Steve Patierno, PhD, Deputy Director of the Duke Cancer Institute, Dr. Bruce Sullenger, PhD, Director of the Duke Translational Research Institute, Dr. Rudy Juliano, PhD, Boshamer Distinguished Professor of Pharmacology at the UNC School of Medicine, and Dr. Jennifer Freedman, PhD, recently promoted to Assistant Professor of Medicine at Duke, thanks in large part to the support of the Peter Michael Foundation.



Duke Cancer Institute UNC (top photo) | Eshelman School of Pharmacy (bottom photos)

(Memorial Sloan-Kettering references referred to on page 2)

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2. Vargas HA, Akin O, Afaq A, Goldman D, Zheng J, Moskowitz CS, Shukla-Dave A, Eastham J, Scardino P, Hricak H. Magnetic resonance imaging for predicting prostate biopsy findings in patients considered for active surveillance of clinically low risk prostate cancer. J Urol. 2012 Nov;188(5):1732-8. doi: 10.1016/j.juro.2012.07.024. Epub 2012 Sep 25.
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4. Donati OF, Jung S, Vargas HA, Gultekin D, Moskowitz C, Zheng J, Hricak H, Zelefsky MJ, Akin O. Multiparametric prostate MRI with T2-weighted, diffusion-weighted and dynamic contrast-enhanced sequences: Are all sequences necessary for the detection of locally recurrent prostate cancer after radiotherapy? Radiology (In press).
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6. Vargas HA, Wassberg C, Fox JJ, Goldman D, Kuk D, Gonen M, Morris M, Scher H, Hricak H. Bone metastases in castrate-resistant prostate cancer: Association between morphological CT patterns, glycolytic activity and androgen receptor expression on PET and clinical outcomes. (Manuscript ready for submission – journal to be determined)

On the cover: Bi-Annual Prostate Cancer Colloquium Attendees

Front row :
1). Samir Taneja 2). Caroline Moore 3). Sarah Crane 4). Veeru Kasivisvanathan 5). Mark Emberton 6). Walter Menzel

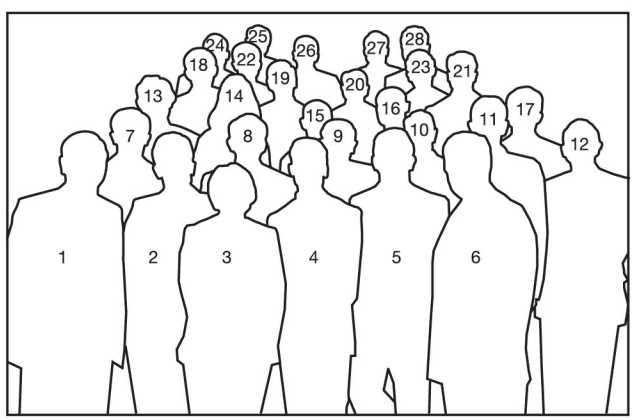
Second row:
7). Robert Grubb 8). Osamu Ukimura 9). Yuji Wantanabe 10). Leonard Marks 11). Laurence Klotz 12). Shonit Punwani

Third row:
13). Scott Eggener 14). Suzanne Palmer 15). Daniel Margolis 16). Phillipe Puech 17). Jurgen Futterer

Fourth row:
18). Boris Hadaschik 19). Arnauld Villers 20). Baris Turkbey 21). Ivo Schoots

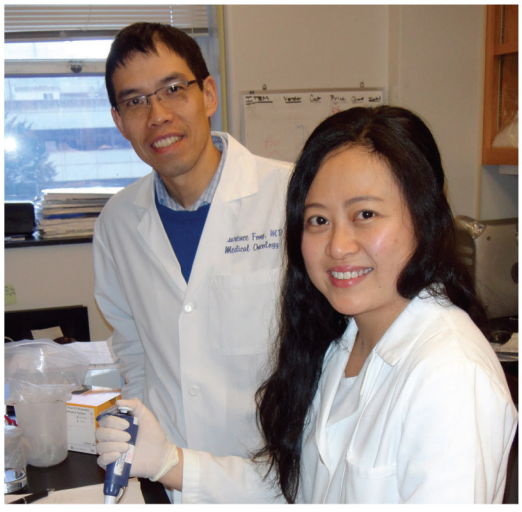
Fifth row:
22). Jonathan Melamed 23). Andrew Rosenkrantz

Sixth row:
24). Richard Simon 25). Gautham Vemana 26). Aytekin Oto 27). Peter Pinto 28). Jan van der Muelen



Next Generation Therapeutic Cancer Vaccines for Prostate Cancer

UCSF Helen Diller Family Comprehensive Cancer Center



Principal Investigator:

Lawrence Fong, MD

Associate Professor, Department of Medicine, Hematology & Oncology

Peter Michael Postdoctoral Fellow: **Serena Kwek,** PhD

Original Proposal

We have discovered that the immune systems in some prostate cancer patients can recognize their own cancer. Tumors, however, can produce different substances and create an environment within the host to dampen these immune responses. By introducing a treatment that can stimulate the immune system, we can drive the immune system to overcome this immunosuppressive milieu, thereby inducing anti-tumor responses. One such approach involves treating prostate cancer patients with both a bone marrow growth factor, GM-CSF, as well as an anti-CTLA4 antibody. The former drug serves to expand the number of cells that serve to educate the immune system, instructing it on what to target. The latter drug releases the brakes on the immune system by blocking one of the crucial immune system checkpoints.

We propose to define the immune targets (antigens) to which patients receiving CTLA4 blockade treatment are responding. Because some patients have dramatic clinical responses and others do not, we can determine whether immune responses to particular antigens are associated with clinical responses or, alternatively, side effects. Moreover, we can determine whether preexisting immune responses to particular antigens could predict who will respond to this treatment. These results could help guide us to select the patients who would derive a clinical benefit from this treatment. Rather than identifying these antigens in animals models, the approach by which most immunotherapies are developed, our proposal focuses on the antigens relevant for prostate cancer patients. *As a result, the antigens that we discover should be immediately relevant for humans.*

Progress Report

We have successfully used a protein array-based strategy to identify immune targets generated by immunotherapy with ipilimumab (anti-CTLA-4 antibodies) in prostate cancer patients. Through this work, we have made some important observations. First, we found that patients by-in-large develop antibody responses to targets specific for each individual, but there are immune responses to targets that are shared between some of the patients. Second, we found that in people who clinically responded to treatment we could generate antibodies to immune targets more frequently than people who did not clinically improve with the treatment. Third, patients who clinically responded tend to amplify pre-existing antibody responses, rather than generating antibodies to new targets. Patients may therefore have specific immune characteristics that could define whether or not they might respond to an immune therapy like ipilimumab. We are now extending our work to examine whether immune responses are also generated to mutated proteins present within the cancer cells. These results would lay the groundwork for develop biomarkers that could predict whether prostate cancer patients might respond to a treatment.