CDMRP
Department of Defense
Prostate Cancer Research Program

PCRP erspectives

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In This Issue

Featured Opinion

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The immune response is divided into two basic components: adaptive immunity, which recognizes specific antigens after immunization, and innate immunity, which acts quickly without immunization. The adaptive immune response, which is divided into cell-mediated (T cell) immunity and humoral (B cell-derived antibody) immunity, comprises the primary focus for cancer immunotherapy.

Cancer immunotherapy is based on the principle that the body's immune system has been honed over the centuries not only to protect one against foreign invaders like viruses and bacteria but also to recognize and attack cells that change from normal cells to cancer cells. Harnessing the power of the immune system to protect against infectious agents has been demonstrated by the successful development of vaccines to virtually eliminate diseases like small pox and polio. Developing immunotherapy approaches to eliminate cancers, however, has been difficult. This is primarily because the body's immune control mechanisms are intended to prevent the immune system from attacking its own cells (including cancer cells). When the body attacks normal

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IMPaCT 2011: Forging Full Speed Ahead to Conquer Prostate Cancer

Excitement filled the air as 825 scientists, clinicians, and prostate cancer survivors and advocates from as far away as Australia and Israel gathered in Orlando, Florida, for the second IMPaCT (Innovative Minds in Prostate Cancer Today) Conference on March 9-12, 2011. These stakeholders met to contemplate the successes of the DOD Prostate Cancer Research Program, to rigorously examine how the program is tackling the challenges still facing patients today, and to set the agenda for prostate cancer research on the near horizon.

Kicking off the conference were Nobel Laureate Dr. Phillip Sharp,[1] of the Massachusetts Institute of Technology, whose discussion illuminated the potential of microRNA—one aspect of RNA science currently being explored—to provide opportunities for innovative prostate cancer treatments, and Dr. Mark Litwin, from the University of California, Los Angeles, who described his pioneering efforts to establish and maintain a California state-funded program for the care of uninsured men with prostate cancer.

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IMPaCT Conference Highlights Advances in Immunotherapy for Prostate Cancer

Immunotherapeutic approaches to prostate cancer treatment have garnered considerable interest from physicians, researchers, and patient advocates since the 2010 approval of sipuleucel-T (PROVENGE®) by the Food and Drug Administration (FDA). The power of the immune system can be harnessed through various strategies, such as the use of cytokines, vaccines, and monoclonal antibodies, and it can be exploited to target prostate-specific molecules. The most well-known molecule is prostate-specific antigen (PSA), which is secreted into the bloodstream and is widely used in prostate cancer screening. Prostate cancer researchers are also developing im-

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VISION: Conquer prostate cancer.
MISSION: Fund research that will end death and suffering from prostate cancer.

» IMMUNOTHERAPY, CONTINUED FROM PG. 1

munotherapies that target prostate-specific membrane antigen (PMSA), prostate stem cell antigen (PSCA), and prostatic acid phosphate (PAP).

The 2011 Innovative Minds in Prostate Cancer Today (IMPaCT) Conference highlighted recent advances in understanding how the immune system interacts with prostate cancer and explored the development of immunotherapies for the treatment of prostate cancer from laboratory to clinical research, including reports on Phase III clinical testing of new therapies.

Dr. Charles Drake, of Johns Hopkins University, gave an overview of the basic science that led to the development of ipilimumab, an antibody against the T cell surface protein, cytotoxic T lymphocyte antigen 4 (CTLA-4), which is currently in Phase III clinical trials for prostate cancer. CTLA-4 is a natural suppressor of the immune response. While this is necessary to prevent immune system overactivity, it can undermine the body's defense against disease. When T cells, which are major components of the body's defense against bacteria, viruses, and cancer, are activated after exposure to small pieces of protein (called antigens) such as PSA, PSMA, PSCA, or PAP, expressed at higher levels in prostate cancer, CTLA-4 provides a "stop" signal to counter the activation (**Figure 1**).

The PCRP supported Dr. Eugene Kwon of the Mayo Clinic in his efforts to demonstrate that blocking CTLA-4 might relieve the stop signal, enabling the generation of a more powerful immune response against the prostate tumor. He presented his early data in a castrated mouse model, which showed that androgen ablation (i.e., removing testosterone) facilitated responses to treatment with anti-CTLA-4 antibody and prevented prostate cancer growth. Moreover, in human prostate cancer Dr. Kwon found that androgen ablation therapy caused an accumulation of T cells in the prostate gland, which he speculated could fuel an immune response that could then be enhanced by anti-CTLA-4 antibody. This led to a Phase II clinical trial in which Dr. Kwon tested androgen deprivation therapy plus ipilimumab in treatment of patients with advanced prostate cancer. Most patients had a 70%-100% response based on the regression of primary and secondary lesions within 3 months of treatment and a downgrade in pathologic tumor stage. These data suggest that androgen ablation may synergize with ipilimumab to elicit an immune response to destroy prostate cancer cells in metastatic prostate cancer, but confirmation in a larger study is needed.

Dr. Celestia Higano, of the University of Washington, described the role of the PCRP-supported Prostate Cancer Clinical Trial Consortium (PCCTC) in accelerating the development of ipilimumab as a treatment for prostate cancer. A Phase I/II dose escalation trial was initiated in 2006 and was expanded to test the drug in combination with a single treatment of high-dose radiation prior to administration of the antibody. A significant number of patients treated with 10 mg/kg ipilimumab responded with a decline in PSA levels, including those with and without prior chemotherapy and/or with or without the radiation treatment. These patients are still being monitored (e.g., therapeutic response, toxicity, and other side effects), but the PSA declines thus far have lasted as long as 14 months. Notably, a patient with metastatic castration-resistant disease experienced a rapid decline in PSA from 655 ng/ml to nearly undetectable levels in less than 2 months, and a large metastatic bone lesion had disappeared by 24 weeks after treatment (**Figure 2**). Based on these results, Dr. Higano concluded that, although ipilimumab is not likely to be as effective in every patient, it can potentiate T cell-mediated responses against prostate cancer. The PCCTC is now enrolling patients in two Phase III clinical trials, testing ipilimumab in (1) a post-docetaxel setting and (2) a chemotherapy-naïve setting.

The PCRP is also supporting Dr. Scott Tagawa of Weill Cornell Medical College, who discussed his work utilizing J591, an anti-PSMA monoclonal antibody linked to a radioactive particle (^{90}Yttrium or ^{177}Lutetium) (**Figure 3**). PSMA is expressed on the surface of virtually all prostate cancer cells, making it an ideal target. In a Phase I clinical trial in patients with advanced prostate cancer, J591 successfully targeted sites of metastatic disease. Slightly better targeting and higher maximum tolerated dose (MTD) was found for ^{177}Lutetium-J591, so Dr. Tagawa moved forward with this antibody conjugate as a single-dose Phase II clinical trial. This therapy was well tolerated by patients and, in addition to its targeting known metastatic sites in 94% (30/32) of patients, other favorable

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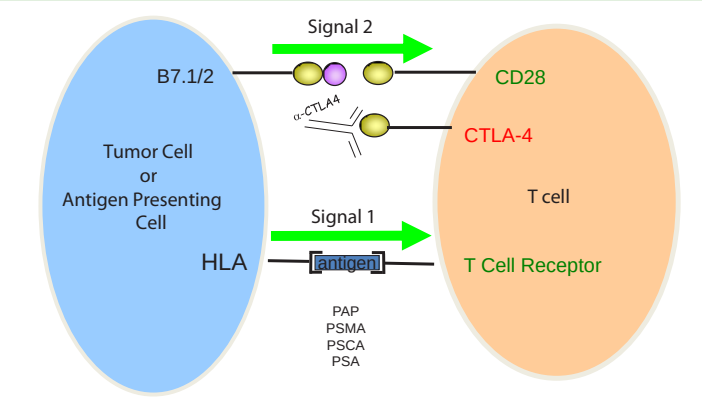

Figure 1: Prostate tumor cells express antigens such as PAP, PSA, PSMA, and PSCA that may be recognized by T cells (signal 1), part of the body's immune system. A second "go" signal (signal 2) must also be triggered to activate an immune response against these tumor cells. In cancer patients, this "go" signal is often hijacked by a natural suppressor of the immune response called CTLA-4, which sends a strong "stop" signal (signal 2) to the T cell, inhibiting an anti-cancer immune response. One promising therapeutic strategy is to block the stop signal with an antibody against CTLA-4 (α-CTLA-4), such as ipilimumab, thereby allowing the "go" signal to proceed, generating a powerful immune response against the prostate tumor.

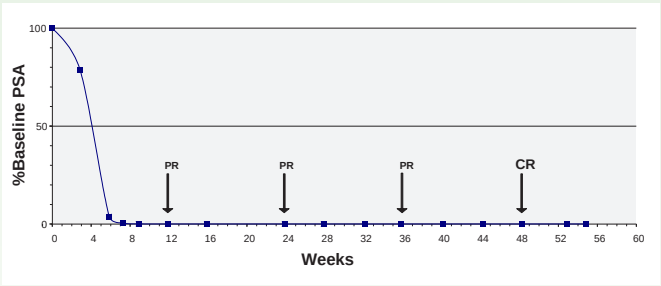

Figure 2: Ipilimumab treatment initiated a rapid decline in serum PSA levels in a patient with metastatic castration-resistant prostate cancer, approaching zero after 8 weeks and remaining stable for 14 months. Partial response (PR) and complete response (CR), meaning complete disappearance of any sign of cancer. Courtesy of Dr. Tomasz Beer, Oregon Health and Science University.

In This Issue

Spotlight

The Future for Prostate Cancer

The 2011 Innovative Minds in Prostate Cancer Today (IMPaCT) Conference closed on March 12 with the "New Horizons" session, a look to the future of prostate cancer research and patient care. Led by Dr. Joel Nelson (University of Pittsburgh), Dr. Oliver Sartor (Tulane University), and Dr. John Isaacs (Johns Hopkins University), experts in the field, participants contemplated the changing landscape, areas of need, and likely breakthroughs in the prostate cancer field over the coming years. Common themes in these talks included the need for increased discrimination between indolent and aggressive prostate cancer, new and improved biomarkers for detection and monitoring of disease, and improved therapy for advanced disease.

Dr. Joel Nelson

Dr. Nelson, a physician-scientist in urology, reflected on the incidence and mortality of prostate cancer and the dire need to improve treatment effectiveness. He projected a sharp increase in prostate cancer incidence as the "baby boomers" approach retirement age and better treatments for other maladies, such as heart disease, are extending life spans in the United States. He warned that morbidity and mortality rates will also rise unless prostate cancer management is improved, especially as there is an anticipated shortage of federal funds to care for these individuals, and he urged all scientists to carefully consider approaches to ensure that their work is aimed at solving the most critical needs in prostate cancer.

Despite these predictions, Dr. Nelson noted that less than 15% of newly diagnosed prostate cancer is deadly and that many men were unnecessarily receiving treatment and suffering from negative side effects. Dr. Sartor, a medical oncologist, elaborated on this point by explaining that prostate cancer is typically so slow-growing that most men diagnosed with the disease die from other causes before their cancer ever becomes a danger to their health, thus emphasizing a critical need for better ways to stratify individual risk.

The most common methods of risk stratification for prostate cancer patients currently include measuring PSA (prostate-specific antigen) levels in the blood and staging the cancer by characterizing the pathological features of the tissue (Gleason score) via biopsy. Improved biomarkers are needed, however, both to better predict who will experience disease progression and to accurately reflect and/or predict therapeutic response.

» continued, **SEE SPOTLIGHT, PG. 5**

Program News

- PCRP FY11 Program Announcements were released on April 22 and May 5 and continued the program's emphasis on fostering new ideas and new investigators for maximal impact on prostate cancer research and patient care. All currently open funding opportunities can be viewed at http://cdmrp.army.mil/funding/pcrp.
- The PCRP has established an aggressive time line to execute the $80 million appropriated by Congress in early April. Scientific peer review of applications will occur from June through October 2011, with hundreds of scientist and consumer reviewers working together to fairly and thoroughly evaluate the merit of every application. Programmatic review will occur in October and December to establish recommendations for funding, ultimately supporting the research projects of highest scientific merit and best designed to accomplish the PCRP goals.
- The PCRP and Prostate Cancer Foundation joined together in celebrating a major outcome of their combined support for the Prostate Cancer Clinical Trials Consortium (PCCTC): ZYTIGA™ (abiraterone acetate, made by Johnson & Johnson) was approved by the Food and Drug Administration on April 28, 2011. This drug was brought through clinical testing by the PCCTC at nearly twice the traditional speed for most drugs, creating an enormous impact for men with metastatic castration-resistant prostate cancer.

Calendar of Events

23: Full applications (by invitation) due for Idea Development and Synergistic Idea Development Awards

1: Full applications (by invitation) due for Clinical Trial, Impact, and Laboratory - Clinical Transition Awards

14-18: AACR Conference on Frontiers in Basic Cancer Research, Intercontinental San Francisco Hotel, San Francisco, California

18-21: AACR Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved, Grand Hyatt, Washington DC

20-22: Summit to End Prostate Cancer, Washington DC. Sponsor: ZERO

22-23: 7th Annual African American Prostate Cancer Disparity Summit, Washington DC. Sponsor: PHEN

Did You Know...

- Approximately 825 people attended the recently held IMPaCT meeting in Orlando, Florida.
- Since its inception, the PCRP has funded 440 new investigators in their efforts to establish themselves in prostate cancer research.
- The PCRP tracks every award from initiation to completion, follow ing up on significant outcomes and ensuring that research advances are communicated to the wider research and consumer communities.
- Every month the PCRP highlights some of the most outstanding research accomplished by investigators on its website at: http://cdmrp. army.mil/pcrp/default.
- The PCRP is the national leader in funding research to understand and ultimately resolve prostate cancer health disparity. With a total PCRP investment of over $30 million, many of these projects can be seen by searching the CDMRP awards database (http://cdmrp.army.mil/search.aspx) under the award mechanism categories of Health Disparity Research Awards and

In This Issue

» IMPACT 2011, CONTINUED FROM PG. 1

L-R Drs. Mark Litwin, Natasha Kyprianou (IMPaCT Co-Chair), and Phillip Sharp, and Mr. Westley Sholes (IMPaCT Co-Chair)

Conferees were then treated to an invigorating session on "game-changing" research in prostate cancer, providing insights into innovative therapies and therapeutic targets and challenging the conventional thinking in the field. Drs. Arul Chinnaiyan, Scott Dehm, Jianfeng Xu, and Muneesh Tewari reported on the genetics of prostate cancer risk, identifying genes, alternative splice variants, single nucleotide polymorphisms (SNPs), and microRNAs, respectively, that are associated with more aggressive prostate tumors and/or may be used for the development of new therapies or diagnostic tests. The high degree of genetic diversity in prostate cancer strongly argues in favor of personalized medicine, and the unique combination of these factors may be the key in predicting the optimum treatment options for each individual. For example, Dr. Chinnaiyan predicted that individuals whose tumors express the transcription factor SPINK1[2] may be more likely than others to respond favorably to treatment with cetuximab, a monoclonal antibody against the epithelial growth factor receptor.

Dr. Eugene Kwon explained the concept of immunotherapy and described the compelling work taking place on the development of ipilimumab (Yervoy™), a monoclonal antibody against the T-cell surface protein CTLA-4. Ipilimumab was propelled into Phase III clinical trials by the Prostate Cancer Clinical Trials Consortium (PCCTC) for the treatment of prostate cancer and was approved in March 2011 by the Food and Drug Administration (FDA) for treatment of advanced myeloma. Drs. Maha Hussain, Charles Drake, and Celestia Higano further detailed the process of taking this new drug from basic research through to Phase III clinical trials.

Drs. Donald Tindall and Howard Scher illustrated the role of the androgen receptor (AR), anti-androgens, and androgen synthesis inhibitors in prostate cancer, and tracked the journey of abiraterone (ZYTIGA™)—a drug that blocks androgen synthesis by inhibiting the enzyme CYP17—from the laboratory to the clinic. Abiraterone was approved by the FDA in April 2011. Dr. Dehm's work on the AR led to the identification of constitutively active splice variants that are missing various segments of the ligand binding domain and are more highly expressed in androgen-independent prostate cancer. Since most of the current anti-androgen therapies target this domain, the presence of these truncated isoforms may explain why androgen-independent cancers are resistant to AR-based therapies. It was with great anticipation, then, that conference participants listened to Dr. Marianne Sadar's presentation of her work on the preclinical development of a promising, first in class, alternative anti-AR drug, EPI-001, which targets the N-terminal domain. Preclinical results have been favorable and efforts are now under way to move EPI-001 into Phase I clinical trials.

Drs. James Mohler and Michael Freeman described the contributions of steroid and cholesterol metabolism to androgen synthesis. In fact, Dr. Mohler challenged the long-standing concept of "androgen-independent" prostate cancer, arguing that the multiple pathways of androgen synthesis prevent a truly androgen-independent state and thus warrant pursuit of more effective mechanisms of inhibition.

In addition, hundreds of scientists showcased their research findings during 7 plenary sessions, 13 symposia with 98 oral presentations, and 646 poster presentations. Consumer advocates and student trainees participated in organized poster tours, led by specialists in each discipline and designed to help consumers and trainees maximize their educational and networking experiences at the conference.

Such educational opportunities were plentiful throughout the conference. Early morning "Meet the Experts" sessions provided a powerful forum for consumer advocates to learn from the field's leading physicians about fundamental principles of prostate cancer, prostate cancer screening, treatment options for localized disease, and quality of life in late-stage disease. In accordance with the PCRP's goal of fostering the next generation of prostate cancer researchers, predoctoral and postdoctoral trainees met with experienced mentors for discussions on mentorship, publishing research, and navigating milestones in their development as prostate cancer researchers. A group of exceptional predoctoral trainees presented snapshots of their research in a "lightning round," and undergraduate participants in the summer training programs networked with investigators from various graduate school programs.

Mr. Robert Young, PCRP Consumer Reviewer, participates in discussion at the 2011 IMPaCT Conference.

The consumer advocates made excellent use of the conference to gain knowledge of advances in research and patient care to take home to their peer communities and also took the opportunity to inspire and challenge the scientists by sharing their personal journeys of overcoming their disease and advocating for research to solve the issues most critical to prostate cancer patients. Dr. Ward "Trip" Casscells, former Assistant Secretary of Defense for Health Affairs and current John E. Tyson Distinguished Professor of Medicine and Public Health at the Texas Heart Institute hailed the PCCTC as the reason that many men in the room were still alive and urged the audience members to continue their support for the PCRP, prostate cancer research, and participation in clinical trials.

The 2011 IMPaCT Conference paved the way for new and stronger partnerships between scientists, clinicians, and consumer advocates. With the support of the PCRP, these determined individuals were infused with renewed zeal and innovative ideas to accomplish their mission of conquering prostate cancer.

[1] *Winner, along with Richard J. Roberts, of the 1993 Nobel Prize in Physiology or Medicine for their discovery of "split genes."*

[2] *SPINK1, while expressed in only 10% of prostate cancers, is associated with their more aggressive forms.*

Prostate Cancer Research Program

For more information:
http://cdmrp.army.mil/pcrp/default

General Questions:
Phone: (301) 619-7071

Application Requirements:
Phone: (301) 682-5507
E-mail: help@cdmrp.org

Consumer Involvement:
Phone: (301) 619-7071
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» SPOTLIGHT, CONTINUED FROM PG. 3


Dr. John Isaacs

Dr. Isaacs, a professor of oncology and urology, agreed that better biomarkers were needed, not only to determine which patients require treatment, but to better customize treatment strategies for individuals. Fortunately, biomarker discovery and development, especially as supported by the PCRP, is currently a very active field. An exciting new concept that has received considerable attention is liquid biopsy, in which circulating tumor cells from individuals are monitored over time to determine when an individual needs to start therapy and to measure a biological response to therapy. Dr. Isaacs argued that this surveillance should also monitor physiological changes that trigger the transition from long-term metastatic disease to terminal disease.

A challenging factor in advanced prostate cancer is the heterogeneous nature of the disease, not only between prostate cancer patients but also within a single patient, who may have several types of lesions at different sites. Dr. Isaacs explained that while a certain therapy may appear to be ineffective, it might in fact be quite effective for a subset of lesions in the patient. For this reason, Dr. Sartor predicted that a cure for prostate cancer would likely require multitargeted therapy. Elucidating further, Drs. Nelson and Isaacs emphasized the critical need for better and more precise imaging techniques that can successfully target cancer lesions while sparing whole glands and organs and minimizing side effects.


Dr. Oliver Sartor

Dr. Sartor discussed the landscape of prostate cancer therapy and the promising new drugs that are being moved through the pipeline. Although the past 2 years have provided much hope with the approval of multiple new treatments that prolong survival by several months (sipuleucel-T, cabazitaxel + prednisone, abiraterone), Dr. Sartor urged the community to do better. He particularly favors targeting the stroma and using novel strategies to disrupt the microenvironment, thereby hindering the growth of cancer cells. Of particular note is the new angiogenesis inhibitor called XL-184, which targets both vascular endothelial growth factor receptor-type 2 and c-met. Bone scans in one patient with metastatic castration-resistant disease revealed nearly complete reversal of bone lesions after 12 weeks of treatment.[1]

Key to advancing new therapies into the clinic is the participation of prostate cancer patients in clinical trials. In fact, Dr. Isaacs hailed these men—who willingly test drugs that might later benefit other men—as his heroes and his inspiration. Jim Kiefert[2] is one such man. A PCRP Integration Panel member and consumer advocate with metastatic prostate cancer, Mr. Kiefert thinks of himself as a warrior, not a survivor. As the final speaker in the New Horizons session, he beseeched everyone to take an active role in the battle against prostate cancer, not just for themselves, but for their sons, their grandsons, and generations yet to come.

[1] *Smith et al. 2010. EORTC-AACR-NCI Symposium on Molecular Targets and Cancer Therapeutics*

[2] *Mr. Kiefert was spotlighted in the February 2011 edition of PCRP Perspectives,Volume 3, Number 1. http://cdmrp.army.mil/pubs/news/pdf/pc_newsletter_Feb2011.pdf*

» IMMUNOTHERAPY, CONTINUED FROM PG. 2

disease responses were observed, including a decrease in PSA levels in 71% of patients receiving the MTD of 70 mCi/m^2. Based on these findings, Dr. Tagawa and colleagues are working on strategies to improve the efficacy of J591 radioimmunotherapy by preselecting patients who are more likely to respond (i.e., higher levels of PSMA expression), altering the treatment schedule, and/or combining J591 radiotherapy with chemotherapy (docetaxel and prednisone) in Phase I/II clinical trials.

Dr. Susan Slovin, of Memorial Sloan Kettering Cancer Center, is also testing the strategy of targeting PSMA in a Phase I clinical trial although with a different approach. A patient's own T cells will be programmed to kill cells bearing PSMA on their cell surface using a retroviral vector encoding a T cell receptor (TCR) specific for PSMA. Recognition of PSMA by the genetically engineered TCR will activate these T cells, which will in turn proliferate and kill tumor cells bearing PSMA.

The IMPaCT Conference also highlighted the discovery of a surprising new target for immunotherapy. Based on previous data in his mentor's laboratory suggesting that some prostate cancer patients (~17%) have pre-existing immune responses to the androgen receptor (e.g., antibodies, antigen-specific CD4+, and CD8+ T cell proliferation, and interferon gamma secretion), Dr. Brian Olson, a PCRP-funded postdoctoral fellow at the University of Wisconsin, presented (1) groundbreaking new data supporting the androgen receptor as a natural target of the immune system and (2) the development of a DNA vaccine targeting the androgen receptor. Dr. Olson demonstrated in animal models that a cytotoxic T cell response can be elicited by direct immunization with a DNA vaccine targeting the androgen receptor, resulting in increased survival times in treated mice. This approach is moving into a Phase I clinical trial.

These projects are just a few of the many ongoing efforts to utilize immunotherapeutic approaches to battle prostate cancer. While these approaches may not be effective for all patients, there is growing support for the idea that a multimodality therapy will be required to cure prostate cancer, and PCRP-supported discoveries in immunotherapy will likely play an integral role.

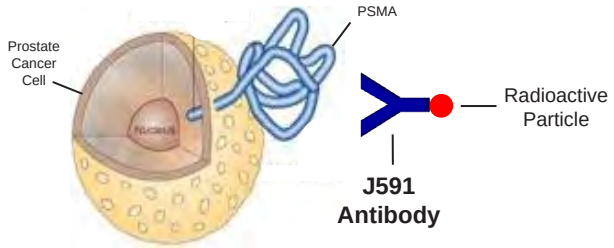

Figure 3: J591 is a monoclonal antibody that specifically binds to prostate-specific membrane antigen (PSMA) on the surface of a prostate cancer cell (bypassing any PSMA-negative cells) and becomes rapidly internalized. The antibody can be "labeled" with a number of agents, including radioactive particles or drugs, which upon binding and internalization may lead to the cell's death. This figure depicts J591 radiolabeled with ^{177}Lu, which is a small radioactive particle. The complex termed ^{177}Lu-J591 has been utilized in a number of Phase I and Phase II clinical trials.

» OPINION, CONTINUED FROM PG. 1

cells, autoimmunity develops. Examples are Type I diabetes (immunity against insulin-producing cells) and multiple sclerosis (immunity against nerve cells).

Immunotherapy treatments for cancer, therefore, not only have to activate the immune system against cancer cells but also must circumvent the body's immune control mechanisms. This complexity has delayed the availability of clinically proven treatments. However, as described in this issue of Perspectives (see "IMPaCT Conference Highlights: Advances in Immunotherapy for Prostate Cancer"), effective treatments are now available and a number of experimental approaches are currently being tested in clinical trials.

Cancer immunotherapy includes active immunotherapy, which requires administration of a vaccine to activate immunity to cancer cells, and passive immunotherapy, which is the delivery of previously developed reagents, like antibodies to cancer cell antigens. Antibodies are produced by B cells after immunization, but they can be produced in large quantities outside the body through specialized genetic processes. These ex vivo-produced antibodies are purified and injected into cancer patients with the intent of directly targeting proteins on cancer cells or to block the function of immune control mechanisms.

In work supported by the PCRP, Dr. Scott Tagawa is studying passive immunotherapy in the form of an antibody to prostate-specific membrane antigen (PSMA) linked to a radioactive agent, which targets and kills prostate cancer cells. In a different twist on passive immunotherapy, Dr. Susan Slovin is using a cell-based protocol in which T cells from prostate cancer patients are genetically modified to target and kill prostate cancer cells.

Active immunotherapy is primarily intended to kill cancer cells through the activation of T cell immunity. The recently FDA-approved sipuleucel-T (Provenge) is a form of active immunity and its effectiveness clearly shows that cancer immunotherapy can help in the treatment of prostate cancer. Dr. Brian Olson is studying a unique active immunotherapy vaccine targeting the androgen receptor in prostate cancer cells. The development of T cell immunity to this antigen may prove to be an effective treatment for prostate cancer.

A treatment regimen was discussed by Drs. Eugene Kwon and Charles Drake that combines active and passive immunotherapy approaches to the treatment of prostate cancer. The treatment involves simultaneously administering a vaccine to activate T cell immunity to prostate cancer cells and an antibody to CTLA4 to block inhibition of an immune response.

Finally, Dr. Celestia Higano described studies that use new antigens produced by the death of prostate cancer cells (resulting from radiation treatment) to activate T cell immunity, followed by enhancement of the immune response by blocking CTLA4 function.

In summary, many immunotherapy approaches are being studied that may provide better treatments for prostate cancer.

Dr. Donald Tindall of the Mayo Clinic speaks with PCRP Fellows at the 2011 IMPaCT Conference.

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

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

http://cdmrp.army.mil/pcrp/default

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Grant Writing Tips

- It is very important that applicants thoroughly **read the Program Announcement before** preparing their applications. Although award mechanism names usually remain the same from year to year, there may be significant changes made each year to the application requirements based in part on changes to the PCRP goals.
- Each award mechanism has its own **eligibility requirements**. Make sure you understand the eligibility requirements before preparing your application. When in doubt, contact the CDMRP Help Desk at 301-682-5507 or help@cdmrp.org.
- Some award mechanisms employ **blinded review** of the pre-application or application to best focus the evaluation of merit on the research idea and strategy. To ensure that your pre-application or application is compliant with the Program Announcement, carefully follow the instructions to sufficiently obscure the identities of the personnel and institution(s) conducting the project.
- After you have prepared your Preproposal Narrative or Project Narrative in Microsoft Word, make sure that the **pdf version** of the document does not exceed the page limitation as specified in the Program Announcement and conforms to the formatting guidelines as specified in the General Application Instructions.
- Good grant writing is easy to read AND **understand**! After presenting your ideas in a clear, descriptive, and specific manner, have a few people in your field (but not working on efforts close to your specific projects) read your pre-application or application, and get honest opinions on its readability. If your readers hesitate in telling you how clear and easy it is to understand, challenge yourself to rewrite until you've achieved maximum clarity!

Watch for more tips in the next issue!

In This Issue