INSIDE THIS ISSUE
- Experimental Vaccine Shows Promise in Prostate Cancer
- Celebrex-Lipitor Combination May Halt Prostate Cancer
- Prostate Cancer Mortality Declining Faster in the United States than in Britain
- Iowa, Arizona Expand on SEA Blue African American Awareness Campaign
- Similar Survival with Salvage Surgery (RP) and Radiotherapy (RT)
- Gene Activity and Cancer’s Racial Divide
- Nanotechnology Enhances Early Detection of Prostate Cancer in Black Males
- The Doctor’s Note
- Protein Identified That Helps Predict Prostate Cancer Survival
- Doc Moyad’s What Works and What is Worthless Column—Probiotic Supplements

June 2008

HOT SHEET

EXPERIMENTAL VACCINE SHOWS PROMISE IN PROSTATE CANCER

Preliminary data presented at the American Association for Cancer Research 2008 Annual Meeting showed a promising synergy when 2 allogeneic granulocyte monocyte colony-stimulating factor (GM-CSF)-secreting prostate cancer cell lines (GVAX) and escalating doses of the anti-cytotoxic T-lymphocyte antigen (CTLA)-4 antibody ipilimumab were combined to treat patients with metastatic hormone-refractory prostate cancer.

“It has become evident to all of us that manipulation of the body’s immune system to attack cancers, as well as to treat and prevent them, is an increasingly viable option in the therapeutic armamentarium,” commented Louis Weiner, MD, director of the Lombardi Comprehensive Cancer Center at Georgetown University, in Washington, DC. “In the past 30 and 40 years, we’ve learned more about the components of the immune system and the way the components integrate to cause an anti-tumor effect.”

The result of this research is that a variety of therapeutically useful agents have been identified. Dr. Weiner pointed out that there are currently 13 approved drugs and treat-

CELEBREX-LIPITOR COMBINATION MAY HALT PROSTATE CANCER

Researchers at Rutgers’ Ernest Mario School of Pharmacy have shown that administering a combination of the widely used drugs Celebrex® (celecoxib, a nonsteroidal anti-inflammatory drug) and Lipitor® (atorvastatin, a cholesterol lowering drug) stops the transition of early prostate cancer to its more aggressive and potentially fatal stage.

Prostate cancer is the second leading cause of cancer death in men in the United States, with more than a quarter-million new cases appearing each year, according to the American Cancer Society. The findings are being presented by Rutgers Professor Xi Zheng at the annual meeting of the American Association for Cancer Research in San Diego, April 14th.

In the early stage of the disease, when it is typically diagnosed, prostate cancer cells depend on androgen hormones, such as testosterone, to grow. Treatment at this stage involves either decreasing the production of the hormone or blocking its actions on the cancer cells. “Anti-androgen therapy slows the prostate cancer but eventually the cancer becomes androgen-

(Continued on page 3)
Recognizing April’s National Minority Cancer Awareness Month, Us TOO International Prostate Cancer Education & Support Network has partnered for the first time with the Iowa Comprehensive Cancer Control Program (CCCP) of the Iowa Department of Public Health (IDPH) and the Arizona Department of Health Services. African American men have the highest rate of prostate cancer incidence in the US. “We greatly appreciate the opportunity to partner with the Us TOO organization to educate Iowans, specifically African American men and families about their high rate of prostate cancer,” according to Holly Smith, Iowa CCCP Coordinator. “Us TOO provided the message and image and CCCP-IDPH created the media campaign; another example of great collaboration between organizations working to conquer cancer.”

The campaign’s message was created by Us TOO International and utilizes poster imagery from Us TOO’s nationwide “SEA Blue” campaign on behalf of prostate cancer patients and their families. SEA stands for support, education and advocacy – the primary components of Us TOO’s mission. Just as pink raises awareness about breast cancer, blue is the color of prostate cancer.

IDPH created the Iowa campaign based on the Us TOO national campaign, which includes 75 billboards in metro Des Moines, Bettendorf/
ments that have clinical benefit and that rely either wholly or in part on the immune system for their anti-cancer activity.

The results of the phase 1 trial showed that the combination therapy lowered prostate-specific antigen (PSA) levels in 5 of 6 patients who received the 2 highest-dose levels of anti-CTLA-4.

Dr. Santegoets and colleagues evaluated the GVAX/ipilimumab combination therapy in 12 patients with metastatic hormone-refractory prostate cancer. All 12 men received a 500-million-cell prime dose of the cellular immunotherapy on day 1, followed by biweekly intradermal administrations of 300 million cells for a 24-week period. The ipilimumab was administered every 4 weeks, beginning from day 1, and the patients were divided into 4 groups, each receiving a different dose of ipilimumab (0.3, 1, 3, or 5 mg/kg). PSA levels fell by more than 50% in 5 of the 6 patients at the 2 highest-dose levels of anti-CTLA-4. Declines in PSA levels were maintained in 4 of the patients for at least 6 months. They also observed resolution of multiple lesions on bone scan in 2 patients and of abdominal lymph node disease in 1 patient; bone pain improved in 1 patient.

The activation of T cells was also monitored to identify changes that correlated with clinical efficacy. Activation of dendritic cells and T cells was noted, and the early data are encouraging, explained Dr. Santegoets. A transient increase was noted in circulating myeloid dendritic cells at the lowest-dose level of ipilimumab (0.3 mg/kg), but not at the 2 highest-dose levels.

“Our research shows that this is a promising approach and we are continuing the study with 16 additional patients,” she said. Dr. Weiner commented that this study is an example of a vaccine that appears to amplify the capacity of the immune system.

**SIMILAR SURVIVAL WITH SALVAGE SURGERY (RP) AND RADIOTHERAPY (RT)**

There are several treatments for localized prostate cancer patients, but no randomized study has compared any RT with RP. Consequently, decisions on local treatment are often based on patients’ and doctors’ preferences and assumptions, explain HG van der Poel and colleagues from the Netherlands Cancer Institute in Amsterdam.

To investigate further, the researchers studied 32 patients who underwent salvage RP and 41 who received salvage RT for cT1c-T2 prostate cancer.

Local biopsy recurrence and a life expectancy of over 10 years was the basis for salvage RP, while salvage RT was performed in patients with a PSA level that had risen above 0.1 ng/ml and no systemic disease. PSA recurrence occurred in 39% of salvage RT patients after an average interval of 38.4 months and in 69% of salvage RP patients after an average of 45.4 months, the team notes in the Journal of Surgical Oncology.

Ten-year PSA recurrence-free survival after primary treatment was nonsignificantly greater in salvage RP patients than that seen in the salvage RT group, at 55% versus 44%. Prostate cancer-specific survival was also nonsignificantly higher for salvage RP, at 93% versus 89% for salvage RT.

PSA recurrence-free survival was predicted by biopsy Gleason score prior to primary treatment and by PSA doubling time prior to salvage treatment on univariate analysis.

The necessity of wearing urinary incontinence pads was less likely with salvage radiotherapy than salvage surgery, at 13% versus 56%, and erectile dysfunction was also less common, at 61% versus 81%.

“This retrospective analysis shows that long-term PSA recurrence-free survival after combined treatment for cT1-2 prostate cancer seems to be independent of the order of radiotherapy and prostatectomy,” the team concludes.

*MedWire News, 10 April 2008*

**GENE ACTIVITY MAY EXPLAIN CANCER’S RACIAL DIVIDE**

Prostate and breast cancer are more deadly for African Americans than for whites. Now it seems that differences in the activity of key genes may be partly to blame.

Black men in the US are around 60% more likely to develop prostate cancer than their white counterparts, and are more than twice as likely to die from the disease. In large part, these differences are thought to be due to socioeconomic factors such as access to healthcare. But at the annual meeting of the American Association for Cancer Research (AACR) in San Diego on 15 April, Tiffany Wallace of the US National Cancer Institute in Bethesda, Maryland, argued that biological differences between the tumours of blacks and whites are also involved.

Wallace and her colleagues used “gene chips” to scan for gene activity in prostate tumours removed from 33 African-American and 36 white patients. There were significant differences between blacks and whites for the activity of more than 160 genes, many of which were involved in regulating the immune system.

These differences could simply reflect greater inflammation in the tumours of African Americans. But given that some of the genes are involved in the production of interferons, one of the body’s defenses against viruses, the higher incidence of prostate cancer in African Americans could be due to a higher rate of infection with an unknown cancer-causing virus. To test this possibility, the researchers are now looking for viral genes in prostate tumour samples.

African American women, meanwhile, are slightly less likely to develop breast cancer than whites—but the disease seems to strike them younger, and is more likely to kill. Differences in gene activity between the tumours of blacks and whites may again be involved, Lori Field of the Windber Research Institute in Pennsylvania told the AACR meeting.

The researchers found 65 genes with significantly different levels of activity between tumours from blacks and whites. Unlike the prostate cancer study, there was no clear link with the immune system. And while some of the genes involved have previously been linked to cancer suppression or tumour development, most had not.

What caused these differences is unclear. “We really don’t know at this time,” Field says. The long-term goal, she says, is to identify new targets for drugs—which could prove particularly valuable in treating African Americans.

*NewScientist.com News Service* 15 April 2008

**NANOTECHNOLOGY ENHANCES EARLY DETECTION OF PROSTATE CANCER IN BLACK MALES**

The emerging field of nanotechnology holds great promise for transforming both cancer research and clinical approaches to care. Researchers here at the American Association for Cancer Research 2008 Annual Meeting reported on the potential use of nanotechnologies to enhance the detection of prostate cancer biomarkers at extremely low levels in blood serum.

Nanotechnology might be useful in developing strategies that will help diagnose prostate cancer at very early stages, which is of particular importance to black men, explained lead author Catherine M. Phelan, MD, PhD, an assistant professor in cancer prevention and control at H. Lee Moffitt Cancer Center & Research Institute in Tampa, Florida.

The 5-year survival rate for black males diagnosed with late-stage prostate cancer is only 29%, whereas patients diagnosed at the early stages have a 5-year survival rate of almost 100%. The prostate cancer mortality rate is also twice as high for black men as it is for white men. “We’re hoping that new technology will have an impact on health disparities,” said Dr. Phelan. “We would like to see a shift to early-stage detection and less morbidity and mortality down the road.”

Nanotechnology has been defined as the interaction between cellular and molecular components and engineered materials, which can, in turn, facilitate (Continued on page 6)
independent, the therapy becomes ineffective and the cancer cells become more aggressive,” said Xi Zheng, assistant research professor at Rutgers, The State University of New Jersey, who conducted the study.

“Treatments available for the later stage cancers are not very good,” said Allan Conney, director of Rutgers’ Susan Lehman Cullman Laboratory for Cancer Research, another researcher on the project. “Oncologists employ classical chemotherapy drugs which are very toxic and don’t work all that well.”

Zheng and Conney’s research objective was to find a way to indefinitely delay the transition to androgen-independence, prolonging the time during which the cancer would be responsive to effective, low-toxicity, anti-hormone therapy.

Zheng explained that their experiments were first conducted on cell cultures in the laboratory, where the researchers tested the effects of the drugs on the growth of prostate cancer cells from four different cell lines. They then moved on to test the drugs on specially bred mice in which prostate cancer tumors were introduced under the skin. Celebrex alone, Lipitor alone, and the two in combination were tested at the lab bench and on the mice.

“A combination of low doses of Lipitor and Celebrex had a more potent inhibiting effect on the formation of later stage tumors than a higher dose of either agent alone,” Zheng reported. “The results from our study indicate that a combination of Lipitor and Celebrex may be an effective strategy for the prevention of prostate cancer progression from the first to the second stage.”

Zheng also noted that the team is exploring the underlying molecular mechanisms to understand how Lipitor and Celebrex work on prostate cancer, perhaps identifying an important signaling pathway for tumor cell growth that the drugs inhibit. Conney pointed out that previous experiments reported in the Sept. 15, 2007, issue of Clinical Cancer Research had demonstrated

“Researchers Skeptical That PSA Screening Saves Lives

Despite major differences between healthcare systems, all-cancer mortality trends in the United States and the United Kingdom were very similar, the researchers note. The main difference appears to be in prostate cancer.

To analyze this difference, investigators used cancer-mortality statistics from Cancer Research UK and the US National Cancer Institute Surveillance, Epidemiology and End Results (SEER) program. They found that age-specific and age-adjusted prostate cancer mortality peaked in the early 1990s at almost identical rates in both countries. However, age-adjusted mortality in the US subsequently declined after 1994, by 4.17% each year (95% confidence interval, –4.34 to –3.99). This was 4 times the rate of decline in the UK after 1992 (–1.14%; range, –1.44 to –0.84). The decrease in the US was greatest and most sustained in patients 75 years or older (–5.32%; range, –8.23 to –2.32). In contrast, by the year 2000, death rates had leveled off in this age group in the UK.

Differences in treatments between the countries might explain some of the divergence in trends, the authors write.

“There is evidence that prostate cancers tend to be treated more aggressively in the US than in the UK.”

Radi cal prostatectomy was more commonly used in the US, for example, even after
This month’s *HotSheet* has several papers with important messages. An interesting report from Oregon found a correlation between an elevated C-reactive protein (CRP), a non-specific measure of inflammation and poor outcome from prostate cancer. Although further studies are needed to substantiate this finding, it poses some interesting questions and opportunities. First, it is unclear at this time how important a predictor it might be. In other words, exactly how many men are identified with this marker beyond other known markers? It could be very predictive but only for a small number of patients. Secondly, if validated, it could present an opportunity for separating patients in future clinical studies by making sure that there is a good balance of men with abnormal CRP levels in each treatment arm otherwise a treatment that is beneficial may fail to be identified.

Another study visits the question ‘which is better, radiation followed by surgery or surgery followed by radiation?’ This very uncontrolled study is really not a valid way to assess the overall impact on survival due to many factors that could be different between the two groups. Even the finding that urinary control and sexual function were better in the men having salvage radiation vs. salvage surgery is open to question. As written, the results would imply that since the survival rates are similar but quality of life is better with salvage radiation, primary surgery is a better course of first treatment. The reader should be aware that any conclusions about this study could be heavily biased because of the study design and only a prospective randomized study can help resolve this debate.

Another study requiring careful interpretation is the report summarizing differences in prostate cancer mortality between England and the US. The study found that over a ten-year period, fewer prostate cancer deaths occurred in the US, which coincided with a much greater use of PSA screening in this country. The authors accurately point out that their findings in no way provide support for screening as a way to lower mortality for several reasons, particularly because prostate cancer mortality also declined in England even without screening. This debate about screening may get resolved soon as randomized screening studies in the U.S. and Europe near completion.

Dr. Moyad again focuses our attention on the ever-increasing use of alternative therapies for almost every disease possible. Patients embrace these treatments because they firmly believe that even if ineffective, there is unlikely to be any chance for significant harm. He cites a recent randomized study using probiotic therapy, or administration of harmless strains of bacteria, to patients with pancreatitis. The study found a significantly higher mortality rate in the group receiving the probiotic therapy. The importance of this article is not whether probiotic therapy should or should not be used for prostate cancer, but rather patients should recognize that unconventional therapies can and do cause harm and they should not be really taken unless tested using well designed clinical studies.

Lastly, a new therapy based on the immune response has some positive preliminary findings. GVAX is a new treatment that had a positive impact on PSA response in a very small group of men with advanced prostate cancer. This treatment is encouraging but preliminary and will require several additional years of study before we know its true impact.

On a different note, last month my new video website containing information about prostate disease was launched <www.chodak.answers.tv.com> and any comments, suggestions or questions are welcomed.

---

**NANOTECHNOLOGY**

(Continued from page 4)

progress in the early detection, diagnosis, and treatment of cancer. A novel approach to increasing the sensitivity and specificity of early cancer detection is through the application of nanotechnology, where luminescent semiconductor nanocrystals or quantum dots (QDs) are conjugated with biomolecules. QDs have unique properties that allow for the long-term immunofluorescence imaging of molecular activities inside living cells.

The goal of their research was to develop a new panel of biomarkers that are sensitive and specific enough to be used as a screening test. Dr. Phelan and colleagues used luminescent QDs to target several established prostate cancer biomarkers, including prostate-specific antigen (PSA), kallikrein 2 (KLK2), kallikrein 14 (KLK14), osteoprotegerin (OPG), antip53Ab, caveolin-1 (Cav-1), and interleukin-6 (IL-6).

Researchers hoped to define the photoluminescence signatures of bound and unbound QDs, which would reflect antigen-antibody complex formation. They could then derive optimal cutpoints for the sensitivity and specificity of novel QD-conjugated biomarkers, both individual and combined, which could be used to detect early prostate cancer in black males.

Using a prostate cancer case-control collection of black males, the researchers observed that bioconjugated QDs displayed an average spectral shift in the maximum position of 4 nm; this shift was not seen in nonconjugated QDs. The researchers noted that the shift is different for each antibody, so each shows a peak at a different wavelength. Peak height represents the amount of protein in the blood sample.

“At the moment, we are optimizing our assay. We want to multiplex our panel and look at more than 1 biomarker” said Dr. Phelan. “An advantage of nanotechnology is that you can detect very low levels of biomarkers, when the tumor is very small, and that is where we want to go,” she added.

*Presented at the American Association for Cancer Research (AACR) 2008 Annual Meeting: Abstract 4741, 15 April 2008.*

*Medscape, 22 April 2008*
PROTEIN IDENTIFIED THAT HELPS PREDICT PROSTATE CANCER SURVIVAL

An Oregon Health & Science University Cancer Institute researcher has identified a protein that is a strong indicator of survival for men with advanced prostate cancer. The C-reactive protein, also known as CRP, is a special type of protein produced by the liver that is elevated in the presence of inflammation.

“This could mean that a simple blood test that is already available could help in clinical decision making and patient counseling. Patients and doctors would know better what to expect from the prostate cancer they are facing,” said Tomasz Beer, M.D., director of the Prostate Cancer Research Program at the OHSU Cancer Institute, associate professor of medicine (hematology/medical oncology), OHSU School of Medicine.

Past research has shown that cancer causes an inflammatory response. This research also suggests that inflammation may play an important role in driving prostate cancer progression and resistance to therapy. Inflammatory cells are attracted to cancer sites and this local inflammation can lead to a release of inflammatory markers, like CRP.

“While inflammation may sometimes slow the progression of the cancer, an increasing body of evidence suggests that cancer can actually take advantage of the inflammatory response, and the reaction of the immune system may fuel cancer progression. To the extent that our hypothesis proves true, C-reactive protein may be reflecting the overall intensity of the inflammation,” Beer said.

The finding that higher CRP is associated with shorter survival and a lower probability of response to chemotherapy is a result of a secondary analysis of inflammatory markers in patients enrolled in the ASCENT study, a large Phase 2 clinical trial that evaluated treatment with docetaxel and DN-101, a high dose formulation of calcitriol or a high dose formulation of calcitriol or

Bottom Line: Even probiotic supplements taken in the wrong situation can be harmful!

Probiotics or “friendly bacteria” are now being offered everywhere. In yogurt, pills, drinks… it is fast becoming big business. However, by introducing friendly bacteria into a person is this really such a healthy thing?!

There are some cases where there is some positive research – for example in children that are placed on antibiotics – but for the most part and with other health conditions, do we know what the heck (notice how I could have used bad language here) we are doing?!! In my opinion, “NO” we do not.

Now, the results of one of the largest randomized trials of probiotic dietary supplements compared to placebo in patients with inflammation of the pancreas is released.1 Approximately 300 patients were tested for only 28 days and took the probiotic twice a day. Patients in the probiotics group had a significant 2.5 times higher risk of death compared to the placebo group!!!

The authors concluded by stating “Most importantly, probiotics can no longer be considered harmless…”

You see, the greatest thing about a pill that has no good evidence is that it has no good evidence. In other words, you can make all sorts of claims and play Monday morning quarterback because all you have are words with no science. Do I think yogurt and other food products that have friendly bacteria are safe?

For the most part I do, but when people start to claim that you should take friendly bacteria in a pill after prostate surgery or radiation or with other conventional therapies, I begin to get nervous. I realize that a man with prostate cancer is not like a patient with inflammation of the pancreas, but I can also tell you that not in their wildest dreams did these researchers think that these friendly bacteria capsules were going to be harmful.

So, the next time someone pushes you to take a probiotic pill for prostate health, please ask to see the HUMAN EVIDENCE and not the test tube or rat evidence! Hey, if you are a test tube or a rat we can cure you of almost anything today. However, if you are a human being your skepticism should run high until someone proves otherwise.

Reference
taking into account the much higher ratio of localized to nonlocalized disease in American patients.

“However,” the researchers point out, “the greater than 20% decline in prostate cancer mortality in the UK in men aged 55 to 74 years began before the increased use of radical prostatectomy and in the absence of screening.” This suggests a role for factors other than increased detection and radical treatment of early-stage disease.

Speaking to Medscape Oncology, Mr. Collins addressed the main limitation of the work. “It is an ecological study in which we have compared 2 populations so it says nothing about individual risk for prostate cancer,” he said. The decline in mortality from prostate cancer in the US is striking in comparison to that in the UK, the researchers conclude. But until publication of additional trials providing robust evidence, we can only continue to speculate about the relative contributions of differences in detection and treatment and the relative balance of benefits and harms.

Medscape, 18 April 2008

**US VERSUS UK**

*(Continued from page 5)*

**PREDICTING SURVIVAL**

*(Continued from page 7)*

docetaxel with placebo. This analysis included patients from both groups. The analyses were supported by Novacea Inc., the sponsor of the ASCENT study. This new finding was in collaboration with Novacea. Because this is the first time CRP has been linked with both response and survival in study subjects with advanced prostate cancer receiving chemotherapy, it will be important to confirm this finding in an independent data set before this can become a routine blood test for men with advanced prostate cancer, Beer explained.

“If confirmed, besides providing useful information for the patient, this finding could also provide us with vital insight into the fundamental role of inflammation in the progression of advanced prostate cancer. A better understanding of this process could provide us with novel therapeutic interventions for control of this disease and its symptoms,” Beer said. Beer’s research was published online in the journal Cancer on April 21st.

ScienceDaily, 23 April 2008

**CELEBREX-LIPITOR**

*(Continued from page 5)*

that the Lipitor-Celebrex combination also inhibited the growth of prostate cancer cells in the later androgen-independent stage.

“So if you can affect the early stage and prevent it from becoming the more severe form, that’s a good thing. If you can also inhibit the growth of the more severe form, that’s also a good thing,” Conney said.

Human clinical trials are being planned at the Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey in New Brunswick. “If the clinical trials go well, we could have something available in five years, but it would be nice to speed that up,” Conney said.

“If the trials show that the drug therapy does a good job of preventing the cancer from advancing, we won’t need to worry about how to handle the more aggressive later stage cancer.

“This is something we hope is going to save lives,” he added.

HULIQ.com, 14 April 2008

**US TOO INTERNATIONAL: OUR MISSION**

Communicate timely, personalized and reliable information enabling informed choices regarding detection and treatment of prostate cancer.

**US TOO INTERNATIONAL**

has received Charity Navigator’s highest rating for the third year in a row for sound fiscal management. Less than 9% of the charities in the US receive this exceptional rating.

---

**US TOO INTERNATIONAL Tax Deductible Donation**

Name: ____________________________ Company: ____________________________

Address: ____________________________________________________________________

City: _____________________________________________ State: ______ ZIP: _____________

Phone: (       ) ____________ Fax: (       ) _____________ e-mail: _________________________

Please accept my enclosed tax-deductible donation to Us TOO a not-for-profit 501(c)(3) organization.

Amount: ____ $25   ____ $50   ____ $75   ____ $100   Other: $ _______     Check # ____________

VISA/MasterCard # ______________________________________ Expiration Date: ____ /____

Signature ________________________________________________________________________

US TOO INTERNATIONAL, Inc., 5003 Fairview Ave., Downers Grove, IL 60515

US TOO INTERNATIONAL, 5003 Fairview Ave., Downers Grove, IL 60515