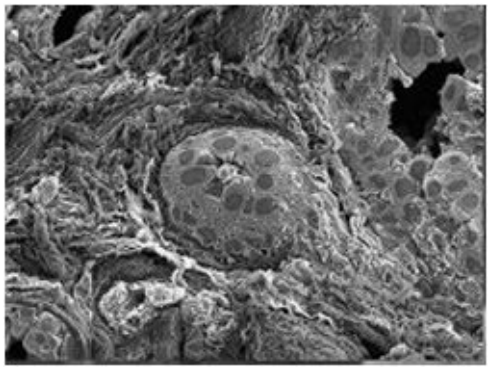
Us Too! Prostate Cancer Education & Support — Know Your PSA

PROSTATE CANCER HOT SHEET

US TOO! INTERNATIONAL — AUGUST 2002

STANFORD RESEARCHERS TRICK CANCER CELLS INTO SELF-DESTRUCTING

STANFORD, Calif. - Researchers at Stanford University Medical Center have tricked cancer cells into self-destructing by briefly disabling a cancer-causing gene. Although the gene revs back up after deactivation, the brief hiatus gives the affected cells a chance to alter their cancerous destiny. This work in mice could open new avenues for treating some human cancers, researchers believe.

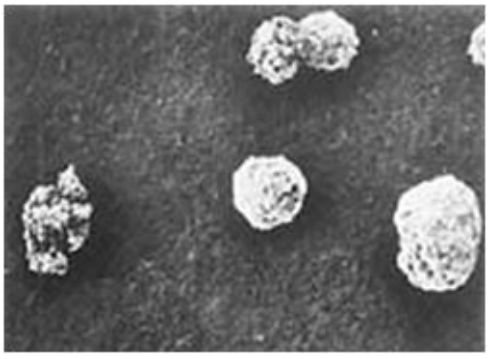


Cancer usually results after a cell accumulates a handful of mutations in cancer-related genes called oncogenes or tumor-suppressor genes. Researchers had thought that cancer cells would side-step attempts to fix any single genetic change, especially after treatment ends. But in a study published in the July 5 issue of Science, researchers found that by briefly tinkering with only one mutant gene they could forever alter the course of the cancer.

"Nobody had ever seen that turning off a cancer gene for a few days caused irreversible change," said Dean Felsher, MD, PhD, assistant professor of oncology and lead researcher on the study. "Most people thought that cancer would come back once treatment that turned off an oncogene stopped."

Felsher and his colleagues worked with a gene called MYC, which normally tells a cell when to grow or divide. In many types of cancers, such as lymphoma, breast, colon, and prostate, this gene produces excess protein that allows the rapid growth characteristic of cancer cells. "Anything you learn about MYC should be applicable to a lot of tumors," Felsher said. He added that because the gene is so important, any results may carry significant weight.

Felsher created bone cancer cells



containing an altered version of MYC that could be shut down by adding a molecular off switch. He then injected those cells into mice, which went on to develop bone cancer.

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NEW SEVEN YEAR CRYOSURGERY DATA RELEASED

In a study released in May 2002, Dr. Duke Bahn of the Prostate Institute of America in Ventura California reviews his results of using cryoablation as primary treatment for 590 patients who had localized prostate cancer. Localized prostate cancer is when all the cancer is contained within or is in close proximity to the prostate and has not metastasized to the rest of the body. The study revealed compelling disease-free results as well as a very high level of patient reported lifestyle satisfaction and positive relationships with their physicians. Equally important, targeted cryoablation of the prostate was shown to be equal to brachytherapy and external beam radiation therapy for low-risk disease, and to surpass published outcomes of radiation therapy for moderate to high-risk disease. (Note that brachytherapy alone is not generally recommended for moderate to high-risk disease, so comparison statistics between brachy and cryo with this population were not available.)

Risk level was determined by PSA, Gleason grade and clinical tumor stage as follows:

1. Low-risk disease is characterized by a PSA of 10 or less, a Gleason grade of 6 or less, and stage T2a or less.
2. Medium risk disease has only one of the following: a PSA greater than 10, Gleason grade greater than 6, or stage T2b or higher.
3. High-risk disease has at least two of the above factors.

Patients at medium risk or those with gland volume greater than 40cc were given pre-operative androgen ablation. Following cryosurgery, no

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PROSTATE CANCER NEWS YOU CAN USE

Us Too! publishes a FREE e-mail based news service which provides updates on the latest prostate cancer related news. To subscribe or link to the archives simply visit the ***Us Too!*** Website: www.ustoo.org

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COMBINED APPROACH IMPROVES PROSTATE CANCER SURVIVAL

Bolla et al
The Lancet
2002; 360:103-108

Disease-free survival rates among men receiving external irradiation alone have been shown to be poor. Previous studies have indicated improved survival in men receiving androgen suppressors alongside radiotherapy, but long-term data have not been available to date. Dr Michel Bolla, from University Hospital in Grenoble, France, and colleagues investigated the outcome of 415 men who underwent external beam radiation to treat their locally advanced prostate cancer between 1987 and 1995. Around half of the men also received subcutaneous doses of goserelin, a luteinising-hormone releasing hormone (LHRH) analogue, every four weeks, starting from the first day of radiotherapy. This treatment was continued for three years. This group of patients also received oral cyproterone acetate for one week before the first radiotherapy day and for three weeks afterwards. All patients were followed up for around five years to determine disease-free rates and overall survival. Seventy-four per cent of men who received combined therapy were disease-free after five years, compared to 40 per cent of those who received radiotherapy alone. Overall survival rates were 78 per cent in the combined group and 62 per cent in the radiotherapy alone group. The researchers conclude that immediate androgen suppression may be a valuable adjunct to radiotherapy for prostate cancer, which alone yields only mediocre results. The optimum duration of androgen suppression has yet to be clarified, however. Dr Bolla said, "Androgen suppression provides a means of improving the outcome of external irradiation alone, by possibly eliminating occult disease." "Moreover, androgen suppression and external irradiation appear to have an additive effect on local disease control by inducing apoptosis," he added.

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PROSTATE CANCER CELL GROWTH INHIBITED BY RED WINE

Romero et al - BJU International
2002; 89:950-954

Studies have suggested that environmental and dietary factors have an important influence on the development of prostate cancer, as witnessed by the higher rate of the malignancy among Japanese men living in the US compared to those in Japan. Mediterranean countries, where red wine is commonly consumed, have lower rates of prostate cancer than other western countries. Dr I Romero and colleagues from Getafe University Medical Centre in Spain investigated five polyphenols - quercetin, morin, rutin, gallic acid and tannic acid - found in red wine to determine whether they exerted an effect on the growth of the LNCaP cell line. LNCaP cells were obtained and cultured in vitro before each of the five polyphenols was added to separate dishes and incubated for 96 hours. Rates of proliferation and apoptosis were assessed using colorimetric and cell-death detection assays, respectively. The cultures were sampled at 24, 48 and 72 hours, and cell proliferation was also assessed after 96 hours. The researchers found that 5 and 10mol/l of gallic and tannic acid and quercetin, and 50 and 75mol/l of morin and rutin, all significantly reduced rates of cell proliferation compared to control plates. Rates of apoptosis inhibition varied between polyphenols, with gallic acid, tannic acid and rutin bringing about significantly greater rates of cell death compared to controls. The effects of morin were only observed at 72 hours, and those of quercetin within the first 48 hours. Dr Romero and colleagues conclude that these polyphenols, which are always present in red wine, significantly inhibit prostate cell proliferation and activate apoptosis. Writing in the BJU International, they add, "These results provide a rationale for studying the in-vivo effects of these nutrients, with the potential for formulating future recommendations about the intake of these substances as chemopreventive agents."

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HIGHLY SPECIFIC TEST FOR PROSTATE CANCER IDENTIFIED

Seabury et al - The Journal of Urology 2002;168:93-99

Previous research has suggested that serum PSA successfully identifies prostatic disease, but is not specific for prostate cancer and may, therefore, lead to many men undergoing biopsies unnecessarily. Dr Charles Seabury and colleagues from Emory University, Northwestern University and West Virginia University investigated

whether specific cell surface proteins or antibodies to these proteins could be identified among cancer patients and controls, and whether this could be a novel means of determining the presence of prostate cancer. The researchers determined 41 cell surface proteins in 25 men diagnosed with prostate cancer and 34 healthy controls. Antibody titres to 67 peptide sequences unique to these proteins were also studied. The levels of peptides in both groups were determined and were classified as being cancer specific, cancer associated or not related to cancer on this basis. The researchers found that three of the peptides assessed were significantly different between the cancer and control groups, with 11 of 25 cancer patients showing positive for this peptide compared to 2 of the control patients (sensitivity 44 per cent, specificity 94 per cent). None of the peptides evaluated were found to generate antibodies in cancer patients alone, although three were found to be cancer-associated. Dr Seabury and colleagues conclude that such tests as that described above may have low sensitivity but high specificity and may, therefore, be a valuable adjunct to PSA testing. Writing in The Journal of Urology, the authors add, "With further expansion of the library based on cell-surface proteins found in various prostate-cancer cell lines, not only could this test be used to identify the presence or absence of known prostate cancer, but it has the potential to correlate with clinical outcomes." "These deglycosylated peptide sequences could serve as targets for anti-tumour monoclonal antibodies or vaccine strategies."

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DOCS MISS CHANCES FOR END-OF-LIFE TALKS

Archives of Internal Medicine 162[11]:1257-1265, 2002

Many patients ask their doctors for help in ending their lives—and physicians then must decide what their response will be. A recent study in Archives of Internal Medicine sought to pick out the points in such discussions that were of help to patients and their families. The team studied 12 patients and their families who seriously were pursuing physician-assisted suicide and 23 families of patients who had sought such help in the past; subjects were recruited through hospices, grief counselors, and patient advocacy organizations. The subjects participated in a semistructured interview that researchers taped and transcribed; the results then were analyzed by a multidisciplinary research team. The team found that patients and family members most valued clinicians' openness to discussing physician-assisted suicide and their ability in dealing with the process and dying; the subjects also valued the ability for clinicians and patients to maintain a relationship, even when they disagreed about physician-assisted suicide. The authors concluded that patients and their families revealed that there are many opportunities to talk about physician-assisted suicide, dying, and care at the end of life that are missed. The researchers wrote that when patients ask about help in committing suicide, doctors need the communication skills to discuss the practice and dying openly. In addition, doctors need to help patients to set reasonable expectations, individualize control of pain, and give patients accurate insight about the ability of medications to end life.

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NEW INTERNAL RADIATION FOR METASTASES IN SKELETAL TISSUE

An early trial of a new type of internal radiation shows promise for treating cancer that has spread to skeletal tissue. The trial results were presented at the 18th International Cancer Congress in Oslo (Norway). Many patients with advanced cancer of the breast, prostate, or lung experience metastasis to skeletal tissue. Current internal radiation therapy is usually based on pharmaceuticals that contain strontium, which has a scope of 6-7 mm and can damage bone marrow and impair the production of new blood cells. In the new study, researchers used a new isotope, radium-223, which has a short scope (2 mm) and a half-life of only 11 days. Early results show that many patients are able to use a lower dose of pain medication. However, a phase II study is needed to perform imaging, determine whether there is any reduction in malignant tissue, and examine pain relief and survival, say the researchers. "We believe this treatment might be administered the first time a tumor spreads to skeletal tissue, and that it might inhibit metastases. This would have an effect on pain and quality of life and could increase survival," says Lise Balteskard, Ph.D., senior medical officer, University Hospital of Northern Norway. Along with doctors at the Norwegian Cancer Hospital, she treated the first patients with radium-223.

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INCREASED TISSUE YIELDED WITH NEW CORE-BIOPSY INSTRUMENT

Hggarth et al,

BJU International

July 2002;Vol 90 Issue 2 :51-55

The research team, from Karolinska Hospital in Stockholm, report increased yield but also report that more biopsies are lost with the new technique compared to the traditional method, however. Previous research has suggested that it is preferable to obtain greater amounts of tissue during biopsy in order to enable effective analysis. However, when a trocar is present, the full diameter of the cannula cannot be filled during biopsy. Dr L Hggarth and colleagues compared the conventional side-notch needle (static stroke length of 22mm and trocar) with a new, single-use, end-cut instrument (stroke length adjustable to 13, 23 or 33mm and no trocar) in 60 men due to undergo octant prostate biopsies. The participants all underwent biopsy of the apex, mid-medial, mid-lateral and basal positions and were randomly sampled on one side using one instrument and on the other side using the alternative instrument. Stroke length of the adjustable instrument was set at 23mm in 40 and 33mm in 20 men. The researchers found that the end-cut instrument provided biopsies 18.4 per cent heavier and 13.7 per cent heavier per length at a stroke length of 23mm compared to the side-notch instrument. Length and weight were 38.4 and 33 per cent greater with the newer technique at a stroke length of 33mm, respectively. In some specimens, the length was actually longer than the notch. However, in more than one-fifth of cases, no tissue was recovered using the end-cut technique compared to less than 2 per cent with the traditional method. Dr Hggarth and colleagues also estimate that the new single-use instrument becomes more expensive than the older method by the time 70 patients have been treated. Writing in the BJU International, they conclude, "At present we recommend the new instrument mainly for situations where there is a suspicion of transition zone canceror cancer in

(continued on page 4)

PROSTATE CANCER NERVE INTERACTIONS IN METASTASIS

Gustavo E. Ayala, M.D.
Baylor College Of Medicine

In prostate cancer, the most common way that cancer cells escape from the prostate (metastasize) is by traveling along the nerve cells. This process, termed perineural invasion, is similar to cars travelling on a highway; the prostate cancer cells travel along nerves that form a path or highway of least resistance. Beyond this purely mechanistic explanation, little is known about how this process occurs.

Researchers at the Baylor College of Medicine are trying to understand this process by studying how prostate cancer cells interact with neural cells. They have demonstrated, with cultured cells, that prostate cancer cells actually cause nerve branches to grow directly toward them, establishing contact between the two cell types.

Once in contact, the cancer cells travel along the nerve branches back to the main body of the nerve where they can metastasize to other parts of the body. It is noteworthy that these cultured cells wrap around nerve cells in the same manner that human prostate cancer wraps around nerves in the prostate.

The researchers also observed that nerves grow more quickly in the presence of cancer cells, and that the prostate cancer cells grow more quickly in the presence of nerves. Such interactions are most likely controlled through chemical signaling pathways that have yet to be discovered.

The researchers intend to further investigate if nerve-epithelial cell interactions are exclusive to prostate cancer, or if they can occur either in cancers of other organs (e.g., the pancreas or colon), or in benign conditions such as those associated with benign prostate hyperplasia.

Understanding the specific mechanisms of these cancer cell/ nerve cell interactions is key to developing therapeutic strategies that target the chemical factors that define the ability of prostate cancer to metastasize.

Publications:

Ayala GE, Wheeler TM, Shine HD, et al. 2001. In vitro dorsal root ganglia and human prostate cell line interaction: redefining perineural invasion in prostate cancer. The Prostate 49:213-223.

This research was funded in FY99 by The Congressionally Directed Medical Research Programs (CDMRP) - Department of Defense (DOD) Prostate Cancer Research Program (PCRP) New Investigator Award of $331,334.00

Genesis and Overview of the Congressionally Directed Medical Research Programs (CDMRP)

The Congressionally Directed Medical Research Programs (CDMRP) originated from a unique partnership among the public, Congress, and the Department of Defense. Grassroots advocacy organizations provided much of the impetus that led to a FY 92 appropriation of $25 million targeted to funding research on the screening and diagnosis of breast cancer among military women and dependents. In response to continuing public requests led by the National Breast Cancer Coalition, Congress appropriated an additional $210 million in FY93. Since that time, the CDMRP has expanded to become second only to the National Cancer Institute as a source of funding for breast cancer research. After noteworthy success in managing the Breast Cancer Research Program, the CDMRP was tasked to manage research programs in defense women's health, osteoporosis, neurofibromatosis, prostate cancer, and ovarian cancer, as well as other specified areas.

Total Congressional appropriations for research for the period of FY92–01: $1.9 billion

Total grants/contracts awarded for the period of FY92–00: 3,516

Anticipated number of awards for FY01: 590

NEWS YOU CAN USE

(continued from page 3)

large prostates. The end-cut instrument can also be considered when it is particularly important to obtain sufficient material for immunohistochemistry."

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INTENSITY--MODULATED RADIATION THERAPY FOR PROSTATE CANCER

Michael J. Zelefsky, Zvi Fuks, Steven A. Leibel
Seminars in Radiation Oncology
July 2002 - Vol12 • #3 • pp 229-37

Intensity-modulated radiation therapy (IMRT) represents a new paradigm in radiation treatment planning and delivery for treatment of prostate cancer with enormous potential. Preliminary data indicate that this highly conformal treatment technique can effectively reduce acute and late-occurring toxicities, improving the quality of life of the treated patient and serving as the optimal dose escalation tool. IMRT produces radiation distributions capable of delivering different dose prescriptions to multiple target sites, providing a new opportunity for differential dose painting to increase the dose selectively to specific, image-defined regions within the prostate. Clinical trials will be necessary to define more clearly the true extent of improved tumor control and reduction in normal tissue complications with IMRT in the treatment of prostate cancer.

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THE MANAGEMENT OF STRESS URINARY INCONTINENCE AFTER RADICAL PROSTATECTOMY

M. Peyromaure, V. Ravery and L. Boccon-Gibod
BJU International
July 2002 - Vol 90 Issue 2: 155

Up to 30% of patients complain about urine leakage after radical prostatectomy, but persistent stress incontinence (beyond 1 year) affects <5% of them. This complication is mainly caused by sphincter dysfunction. Some preventive measures have been described to decrease the risk of incontinence after radical prostatectomy, but with conflicting results. The effectiveness of preoperative and early postoperative physiotherapy is controversial. Moreover, while meticulous apical dissection of the prostate significantly improves

postoperative continence, the benefit of other surgical techniques, e.g. preserving the bladder neck and the neurovascular bundles, is under debate. The treatment of persistent stress urinary incontinence is mainly based on surgery, as this type of incontinence usually does not respond to physiotherapy and anticholinergic medication. While injection therapy is safe and well tolerated, its effect on postoperative continence is limited and decreases with time. The best results are achieved by implanting an artificial urinary sphincter, but with significant complication and revision rates.

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MEN'S HEALTH CONCERN
BBC News Online

Health experts warn that men are being condemned to an early grave because of neglect and a health bias against them. There are no routine cancer screening services for men, whereas women are screened for cervical and breast cancer.The Men's Health Forum says there has been no general improvement in men's health over the last three decades, and in some conditions, such as testicular cancer and liver disease, the situation has become worse. The Men's Health Forum is launching a consumer health website for men at the start of their National Men's Health Week www.malehealth.co.uk

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ODE TO SOY: SALES OF THE BEAN HAVE EXPLODED, BUT ARE ITS HEALTH BENEFITS BEING OVERSTATED?
New York Times

HEALTH CLAIM: Prevents prostate cancer.

REALITY: Early studies show promise that eating soy can reduce the odds of getting prostate cancer. Some scientists have raised concerns that soy could have an adverse effect on the body's hormones and increase the risk of cancer because isoflavones act as a weak form of estrogen. In approving health claims for soy on food labels, the FDA differentiated between soy protein, where the benefits are backed by dozens of clinical trials, and soy isoflavones, where debate continues. The FDA extended the health claim to soy foods, but did not include dietary supplements that isolate isoflavones. Dr. Michael Hirt, director of the Center for Integrative Medicine at Encino-Tarzana Regional Medical Center, advises his patients against taking isoflavone tablets, saying more research needs to be done. He does advocate a diet with moderate amounts of soy foods. "There have been some studies giving animals high unnatural doses of soy, things you can't imagine a human coming close to consuming," Hirt said. "There are no studies showing normal human consumption of two to four servings a day would have any detrimental effect." Experts say those in good health should strive for 15 grams, or two servings per day, to receive the nutritional benefits of soy. When shopping for soy products check the labels for soy protein. Condiments like soy sauce don't contain the powerful punch of soy protein products. The easiest way to add soy to your daily diet is at breakfast, by choosing soy milk and soy-based cereal. For mainstream tastes, Messina also likes the freshness and convenience of edamame, the green vegetable soy pods. At Japanese restaurants, they're served boiled and salted. But they also make a tasty addition to stir-fries, rice dishes and pasta dishes. Edamame, shelled and unshelled, can be found in the freezer section of most supermarkets. For cooking, tofu and soy milk are the most versatile items, said Patricia Greenberg, host of "Local Flavors" on California State University, Northridge's KCSN 88.5 FM and author of several soy cookbooks. Soy milk can take the place of milk or cream in any recipe. Substitute tofu for eggs, meat and cheese, said Greenberg, who also teaches local classes on cooking with soy. "People turn up their noses at it, but some of the soy products are just fantastic," Greenberg said. "You don't need to throw out everything in your refrigerator. Treat soy as an ingredient."

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NO INCREASED RISK OF PROSTATE CANCER POSTVASECTOMY
Journal of the American Medical Association (287:3110-3115, 2002)

Many men elect to undergo vasectomy as a means of contraception, although they may harbor the fear that the procedure can cause prostate cancer. Scientists at New Zealand's Dunedin and Wellington Schools of Medicine found that vasectomy does not increase the risk of prostate cancer, even 25 years or more after the procedure was performed.

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STEM CELL INJECTION OFFERS HOPE FOR PROSTATE PATIENTS

Doctors say prostate cancer patients could be saved by an injection of blood cells from their sibling. The first patient to have the treatment was given six months to live but is still alive 15 months later. The Daily Mail says his prognosis has dramatically improved. The treatment centres on stem cells, which can develop into any kind of tissue. Dr Ulf-Henrik Mellqvist, of the University of Gothenburg, says cells from a sibling could become cancer-fighting immune cells when injected into prostate patients. The findings were unveiled at the congress of the European Haematology Association in Florence. "It is impossible to kill prostate cancer cells with chemotherapy and radiotherapy," he said. "It is traditionally treated with hormones or castration, but the benefits of these treatments are transient and when they disappear, there is nothing more you can do. "We had the new idea of making an effort to attack tumours using immune cells from a donor source. It is a totally new concept." The first patient to have the procedure had tumours all around his body. His sister was tested and found to be a match - siblings have a 25% chance of matching. He suffered some side effects to his gut and skin, but the cancer responded almost immediately. Some tumours completely regressed while others stabilised.

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THE VALUE OF PSA MARKERS

Prostate specific antigen (PSA) has revolutionised the early detection of prostate cancer and enables tumours to be detected between five and seven years before they become palpable. However, the ability of the various PSA markers to distinguish malignant from benign prostate lesions is limited. Chair of the meeting Professor Louis Jean Denis said, "PSA is, on paper, the best marker, but in practice, we need a better one." Dr Hans Lilja, from Lund University Hospital in Malm, Sweden, gave an outline of the value of the currently

(continued on page 6)

available biological PSA forms and speculated on the future of prostate cancer detection. He said that measurement of free-to-total, or complexed, PSA enhances the diagnostic specificity by between 20 and 40 per cent over total PSA testing, with only a 5-10 per cent loss in sensitivity. But he cautioned that free-to-total PSA enhancements might be limited due to shorter in-vitro stability of free compared to complexed PSA, which requires strict pre-analytical sample handling, and by severely impaired renal function because the free PSA is eliminated by glomerular filtration. According to Dr Lilja, data suggests that complexed PSA might replace total PSA as the first-line test for the work-up of men with suspected prostate cancer. "From this measurement it could then be decided whether or not to perform additional testing for proportions of free-to-complexed PSA to further enhance the diagnostic specificity," he said. In a population study at Lund University, involving 438 men who went on to develop clinically significant cancer 20 years later and 1,386 age-matched controls, baseline levels of free and complexed PSA and the exogenous prostatic protease human kallikrein 2 were significantly higher in the cancer group than in the control group. Dr Lilja said the finding of significantly elevated plasma levels of total, complexed and free PSA, plus lower percent free PSA in men later diagnosed with prostate cancer compared to men without this malignancy suggests that, "we might develop far more optimal algorithms to identify men at risk of developing clinically significant prostate cancer long before it becomes incurable". He said that future studies might focus on "nicked" PSA (PSA that is inactivated by internal peptide bond cleavage) and intact PSA for diagnosing prostate cancer. Source: 18th UICC International Cancer Congress, Oslo, Norway

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RESEARCH INTO PROSTATE PATIENT DISTRESS URGED

Bisson et al

BJU International 2002; 90: 56-61

The study's authors, from the University Hospital of Wales, aimed to determine the level of psychopathology, traumatic distress and quality of life among men with newly diagnosed, clinically localised prostate cancer. They wished to look at the effect of a consultation in a combined specialist early-prostate cancer clinic on these factors and also to determine predictors of psychopathology. Eighty-eight patients were quizzed about their psychological health and asked to complete a patient-satisfaction survey. The levels of psychopathology varied according to the type of scale used but ranged from 0 to 14 per cent. Generally, anxiety and traumatic stress symptoms were found to be more common than those indicating the presence of depression. Quality-of-life scores showed a relatively good level of functioning and pre-morbid factors and disease status did not predict psychological distress. Younger age was "mildly predictive" of poorer psychological functioning. Following a joint clinic appointment anxiety symptoms fell slightly but depressive symptoms showed a slight increase. "This study suggests that men with early localised prostate cancer have low levels of psychopathology overall," concludes the research. Research is needed to help develop guidelines regarding the best ways of offering help to men displaying signs of psychopathology, add the authors of the study.

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RETURN OF PROSTATE CANCER FIRST SEEN BY MRI, NOT BIOPSY

A study has found that dynamic magnetic resonance imaging (MRI) can detect prostate cancer recurrence even before it can be detected by biopsy. The finding was presented at the annual meeting of the American Roentgen Ray Society in Atlanta (GA, USA). The study, conducted by researchers at Sapporo Medical University (Sapporo, Japan), involved 21 patients who had a rising prostate-specific antigen (PSA) level following radical prostatectomy. All patients had an ultrasound-guided biopsy that came back negative, but the MR images in 17 of the 21 patients indicated local recurrence. Additional biopsies to confirm recurrence would have wasted precious time, during which patient PSA levels would have continued to rise. Therefore, the researchers conclude that prostate cancer patients with a rising PSA following prostatectomy should first have an MRI to determine if their cancer has returned. "MR is allowing us to detect the recurrence earlier, when the cancer can be more effectively treated with radiation therapy," says Miki Takeda, M.D., the lead author of the study. In fact, 15 of the 17 patients in the study were treated with radiation therapy, and seven are now considered cancer free. "Dynamic MR imaging contributed to these results," adds Dr. Takeda.

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EARLY HORMONAL THERAPY BENEFICIAL FOR RADICAL PROSTATECTOMY PATIENTS

New data indicates that prostate cancer patients who have had radical prostatectomy benefit significantly from early hormonal therapy. Hormonal therapy given for prostate specific antigen (PSA)-only recurrence prior to objective progression significantly extends progression-free survival. The results are based on data in high-risk patients from the Department of Defense (DoD) Center for Prostate Disease Research (CPDR) and were presented at the American Urological Association's annual meeting in Orlando, Florida.

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PROSTATE SURGERY PRESERVES POTENCY, BUT HMOS ARE PUTTING UP BARRIERS

Wall Street Journal
June 19, 2002

People contract with HMOs knowing that they are more restrictive than other forms of insurance. But whether an HMO meets its contractual obligations if its network doctors can't come close to matching the results of other surgeons is a tough question to answer "There is no legal or contractual requirement that the Health Plan send their members to an academic medical center or to an out-of-plan physician who has performed more procedures than a qualified physician," View the complete article (including the diagrams and chart of surgeon outcomes): http://ustoo.org/WSJ061902.pdf

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SCIENTISTS DEVELOP "CANCER-FIGHTING" TOMATO

Nature Biotechnology

The discovery came by accident after scientists from Purdue University in Indiana and the US Department of Agriculture's (USDA) Agricultural

Research Service sought to develop tomatoes for food processing that were higher quality and would ripen later. Lycopene is an antioxidant found in tomatoes that gives them their characteristic colour. The chemical has been the focus of much attention since a six-year study of nearly 48,000 men, by Harvard University, found that those who ate at least 10 servings of food a week containing tomatoes were 45 per cent less likely to develop prostate cancer. Further research also found that lycopene reduces blood levels of oxidised low-density lipoproteins, commonly known as "bad cholesterol", therefore reducing the risk of heart disease. However, despite these benefits it is difficult to increase amounts of lycopene in the diet because purified antioxidants taken as dietary supplements do not seem to work, explained Randy Wilson, director of agricultural research programmes at Purdue University. The developers of the new tomato, Professor Avtar Handa and Dr Autar Mattoo, who heads the USDA vegetable laboratory, say the discovery could provide a natural source for increased dietary lycopene. They found that lycopene levels were increased between 2 and 3.5 times that of tomatoes that had not been genetically engineered. "This is one of the first examples of increasing the nutritional value of food through biotechnology," said Prof Handa. "In fact, it may be the first example of using biotechnology to increase the nutritional value of a fruit."

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PROSTATE TISSUE COULD TREAT BONE DISEASE

The Prostate

A team from Ohio State University's Comprehensive Cancer Center point out that, unlike other cancers, when prostate cancer spreads to the bones it stimulates growth. When most other cancers spread to the bones, they cause them to crumble, resulting in pain and debilitation. Dr Tom Rosol, a vet at the centre, says that up till now it has been difficult to find out why prostate cancer has this effect on bone because of the problem of finding a suitable animal model. Whenever scientists put human prostate cells into animals they behave differently to the way they do in humans, he says. He decided to test whether healthy prostate tissue, in addition to cancerous tissue, was capable of sending growth signals to the bone. And he used dogs' healthy prostate tissue as a means of testing his hypothesis as they are the only animals, other than humans, that develop cancer of this gland. Small amounts of prostate tissue obtained from dogs were inserted under the skin of adult nude mice, which were observed for two weeks. The results left researchers "shocked", says Dr Rosol. Within two weeks the density of the skullcap or calvaria of the mice had almost doubled. "This was really exciting, not just because of the speed of the reaction, but because there are really very few things in nature that induce bone growth," says Dr Rosol. While he says it is unclear what causes the bone to form he suggests the probability is that it is a "complex mix of growth factors", such as a parathyroid hormone-like protein and endothelin-1, which act alongside receptive agents in the hosts' bone. His team is currently working with a drug designed to block endothelin-1 activity and they believe it may be working. Dr Rosol says that there is a need to develop new and workable animal models to improve understanding of cancer. But he says that a process such as prostate cancer metastasis may hold the clue to an effective treatment for diseases such as osteoporosis that involve bone destruction. "What is devastating for a prostate cancer patient may be a source of hope for someone with osteoporosis," adds Dr Rosol.

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SCIENTISTS HOPE PROTEIN IS THE TAP TO TURN OFF TUMOUR GROWTH

Sydney Morning Herald - 7/15/02

British scientists have stumbled on what could be the body's secret weapon against cancer a protein that has the power to starve tumours by blocking their blood supply. Researchers believe the protein may be effective against a wide range of cancers and lead to the design of fundamentally new anti-cancer drugs. The molecule is a special form of a protein called vascular endothelial growth factor (VEGF), which promotes angiogenesis, the growth of blood vessels which feed tumours. Usually it is only seen in diseased tissue, but it also occurs in healthy kidneys where it does not seem to generate tumours. When scientists led by Dave Bates and Steve Harper of the University of Bristol questioned why, they discovered a different form of VEGF, called VEGF 165b, which inhibits the original VEGF and prevents angiogenesis in the kidney. They believe the protein could also combat the development of breast, lung and prostate cancer. It may also help in the treatment of atherosclerosis narrowing of the arteries and diabetes, where VEGF also plays a role. Dr Bates, whose work was published yesterday in the journal Cancer Research, said: "Every cancer known uses VEGF to make new blood vessels. Even with a blood cancer like leukaemia there are tumours which grow in the bone marrow." Australian researchers reacted cautiously to the find yesterday, saying similar anti-angiogenic agents had been tested in clinical trials to little effect. Richard Kefford, director of the Westmead Institute for Cancer Research, said preliminary trials of synthetic anti-angiogenic drugs, including thalidomide, had been disappointing. The new protein was an important discovery in a "hot" field of cancer research, but potential therapeutic benefits were speculative at best, he said. "There's been a steady stream of these sorts of discoveries," Prof. Kefford said. "They're all contributing to the great tapestry of cancer research and each one has some potential." Elizabeth Musgrove, a senior cancer researcher at the St Vincent's-based Garvan Institute, said while any new anti-angiogenesis agent would need to undergo trials in a human-model tumour, publication of the discovery was a measure of its significance. "This is published in a top cancer research journal ... but there's still a long way before you can say this is going to be a new therapy," Dr Musgrove said. "But it's an interesting find."

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YOUNG CIGARETTE SMOKERS HAVE MORE AGGRESSIVE DISEASE

Few people make the link between cigarette smoking and prostate cancer. But the habit is linked to aggressive forms of prostate cancer, according to a new study conducted by William W. Roberts, MD, of the Brady Urological Institute at Johns Hopkins Hospital in Baltimore, MD and presented at the annual scientific meeting of the American Urological Association (AUA) in Orlando, FL

Seven Year Cryosurgey Results

(continued from P. 1)

other treatment was given. Follow-up included regular PSA testing as well as biopsy at 6, 12, 24 and 60 months, or if the PSA rose above 0.5ng/mL. All patients completed questionnaires regarding complications at each follow-up visit. Patients were followed for up to nine years after surgery.

The definition of clinical success used by the authors to compare their outcomes to those of patients treated with brachytherapy and external beam radiation therapy was the standard criteria used by the American Society for Therapeutic Radiology and Oncology (ASTRO). By this criterion, three successive rises in PSA indicates recurrence (treatment failure) and patients in whom this in not observed are considered "biochemically disease free". In other words, the PSA may fluctuate as long as it doesn't rise three times in a row.

Using ASTRO, the seven year disease-free success statistics reported in this study of cryosurgery were:

1. 92% success in low-risk patients
2. 89% success in medium-risk patients
3. 89% success in high-risk patients.

In other words, men with early stage tumors and low-risk disease can expect roughly equal success among cryosurgery, RP, brachytherapy and RP (EBRT has somewhat lower success rates.) However, for men with medium to high risk tumors, minimally invasive cryosurgery appears to achieve better long-terms results than those published for other treatments. The ability of cryosurgery to destroy microscopic cancer involvement in locally advanced disease thus increases the odds of patient survival.

The authors clarified their diagnostic strategy by using color Doppler ultrasound to locate and stage the tumor precisely, ultrasound guidance in placing the freezing probes, thermocouples to monitor temperature within and around the gland, a urethral warming catheter, two freeze-thaw cycles and overnight inpatient observation.

Finally, in tallying the follow-up questionnaires, the authors found that patients reported no serious complications and the lowest rate of urinary incontinence as compared to radical prostatectomy and radiation therapy (4.3% defined as the use of any pads). Patients also reported the highest level of satisfaction with their doctors, compared with other treatments. This is often regarded as a marker of quality of life, since patients whose lifestyles have diminished as a result of treatment often report less satisfaction with their caregivers. In conclusion, the seven-year data of Dr. Bahn and colleagues demonstrates the long-term safety and efficacy of cryosurgery in destroying prostate cancer, avoiding the risks of surgery and radiation, and preserving quality of life.

Researchers Trick Cancer Cells

(continued from P. 1)

When he fed mice the off switch, MYC production stopped and the cancer cells quickly reverted to normal bone cells. After 10 days, he stopped treatment, allowing the gene to resume churning out protein. Instead of restarting cancerous growth, the cells died.

Mice that had their MYC gene switched off for 10 days survived four times longer than untreated mice with bone cancer. The cancer resurfaced in some of the treated mice, but went back into remission with another round of temporary MYC-disabling treatment. "You don't always need to shut the oncogene off permanently," Felsher said. "That could change the way you think about treating cancer."

Felsher cautioned that his current results may not apply to all cancers. His previous work shows that MYC — like all oncogenes — is a complicated gene that can contribute to cancer by many different mechanisms. Depending on which role the gene is playing in the cell, the effects of shutting it off may vary. "We are trying to understand the genetics of when shutting off MYC will work," Felsher said.

Source: Stanford University

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