As part of our continuing Bone Health awareness campaign, Us TOO is pleased to announce a free Bone Health informational teleconference program scheduled for Thursday, January 20, 2005 at 6PM Pacific, 8PM Central and 9PM Eastern time. Highlighting this program will be the participation of Stephen Strum, MD, a medical oncologist specializing in prostate cancer and a recognized expert in disorders involving bone. This 50-minute program, includes Bill Blair, a prostate cancer patient knowledgeable in the field of Bone Health and having personally faced such issues with great success. Mr. Blair is also a highly regarded patient advocate, and a long time consultant and educator. The Bone Health teleconference will also feature a Question & Answer session where you can ask questions of Dr. Strum and Mr. Blair.

(Continued on page 2)

The polyphenols present in green tea help prevent the spread of prostate cancer by targeting molecular pathways that shut down the proliferation and spread of tumor cells, as well as inhibiting the growth of tumor nurturing blood vessels, according to research published in the December 1 issue of Cancer Research.

A team of researchers from the University of Wisconsin, Madison, Wis., and Case Western Reserve University, Cleveland, Ohio, documented the role of green tea polyphenols (GTP) in modulating the insulin-like growth factor-1 (IGF-1)-driven molecular pathway in prostate tumor cells in a mouse model for human prostate cancer. “Consumption of GTP led to reduced levels of IGF-1,” said Hasan Mukhtar, Ph.D., Dept. of Dermatology at the Univ. of Wisconsin, the senior author of the paper.

(Continued on page 4)

Lorus Therapeutics has initiated a clinical trial of GTI-2040, its antisense drug, in combination with docetaxel and prednisone in hormone refractory prostate cancer (HRPC) at Princess Margaret Hospital in Toronto.

This is the sixth and final clinical trial sponsored and funded by the U.S. National Cancer Institute (NCI) under a clinical trials agreement between Lorus and the Cancer Therapy Evaluation Program of the Division of Cancer Treatment and Diagnosis, NCI.

The study includes detailed assessments of metastatic disease as well as pharmacokinetic and pharmacodynamic parameters, following the safe recommended Phase II dose for GTI-2040 and docetaxel in combination for non-small cell lung and prostate cancers.

In addition to HRPC, the decision was made to proceed with the
US TOO PUBLICATIONS

In addition to the Hot Sheet, US TOO offers a FREE e-mail based service called NEWS You Can Use sponsored by Sanofi, providing updates on the latest prostate cancer related news. To subscribe or link to the archives, simply visit the Us TOO website www.ustoo.org.

Items contained in Us TOO publications are obtained from various news sources and edited for inclusion. Where available, a point-of-contact is provided.

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NEW US TOO INTERNATIONAL BOARD OF DIRECTORS AND OFFICERS APPOINTED

At the recent December 4, 2004 meeting of the Board of Directors important transition issues took place. First, the Board had to say farewell to Lew Musgrove who will be leaving the Board and retiring as Chairman at the end of this year. The Board did take time to recognize his efforts and gave him a special “Thank You” for his years of service and leadership.

To assure continued leadership the Board formally appointed a slate of new officers and four new members for the Board.

Joe Piper the Chair of the Board Membership Committee presented the recommendations to the Board after an intensive review of a long list of impressive candidates.

Acting on Joe’s suggestion, the Board and staff will examine ways to utilize the assistance and talents of those we were not able to appoint at this time. The Board recognizes we are very fortunate to have had so many talented and motivated people seek these positions.

Chris Bennet from Illinois, Carl Frankel from Pittsburgh, Bill Palos from Illinois and Jim Raby from New Orleans will assume their new roles on January 1, 2005 and will attend orientation that month.

Also, reappointed to the Board were Greg Bielawski from Illinois, Don Lyman from Kentucky and Harry Pinchot from California.

The new Officers of the Board for 2005 are Jim Kiefert as Chairman from Washington state, Don Lyman as Vice-Chairman, Jo Ann Hardy as Secretary from Detroit and Greg Bielawski as Treasurer.

We plan to feature each of our 15 Members of the Board as we go this year, so look for information in future editions of the HotSheet.

ANTISOMA’S TELOMERE-TARGETING AGENT BLOCKS EXPERIMENTAL PROSTATE CANCER

UK biotech company Antisoma said on Thursday new data showed that one of its telomere-targeting agents (TTA) rapidly blocks prostate tumor growth in a human xenograft model.

"While in untreated control animals tumors grew to lethal size within 10 days, animals given the TTA experienced a halt in tumor growth at around day 7 and survived to the experiment's end on day 25," the company said in a statement.

Antisoma's head of research, Lloyd Kelland, said: "What's really exciting about these TTAs is the speed of their anti-tumor effects. We're not having to wait for many rounds of cell division before the effects kick in, which was a major concern with earlier drugs that were pure telomerase inhibitors."

Clinical trials should begin by 2006, a company spokesman said.

Reuters Health, 4 November 2004

BONE HEALTH

(Continued from page 1)

The teleconference is part of a broader campaign to bring greater awareness about the issue of bone health, especially as it relates to Prostate Cancer. In November, an excellent brochure about Bone Health was added to the Us TOO website's Resources/Downloads section and will soon be available in a printed version. Funding for this Bone Health program and brochure came from Novartis Oncology, and was produced in cooperation with the American Foundation for Urologic Disease (AFUD).

To participate in the “live” call, dial 1-800-437-2398.
HEALTH DISCOVERY CORPORATION
ANNOUNCES DISCOVERY OF NEW GENE BIOMARKERS FOR BPH

Health Discovery Corporation (OTC Bulletin Board: HDVY) today announced the discovery of a new set of genetic biomarkers that are expected to lead to significant improvement in the diagnosis and treatment of Benign Prostatic Hyperplasia (BPH).

This set of newly discovered genetic biomarkers was able, with a high degree of accuracy, to separate BPH (Benign Prostatic Hyperplasia) from prostate cancer. These biomarkers were also shown to separate BPH from normal with a high degree of accuracy. This indicates that BPH is a disease with molecular characteristics of its own. This new discovery could be used to develop a new non-invasive diagnostic test for BPH, which does not yet exist, as well as a complementary type of therapy for patients with this disease.

BPH occurs in approximately 25% of men over the age of 40, 50% of men over the age of 60, 80% of men over the age of 80, and 90% of men over the age of 85. The enlargement often leads to obstruction of the urine flowing through the prostatic urethra.

Of the 9 million cases of BPH in the United States, 2 million receive drug therapy treatment while an additional 7 million are “watchful waiters,” men who are waiting for new treatments. BPH is a common condition, representing a $3 billion annual market in the United States alone.

Dr. Herbert Fritsche, Professor and Chief of Clinical Chemistry at M. D. Anderson Cancer Center stated, “This exciting new gene discovery could provide the vital information necessary to create a completely new drug to treat this extremely common disease. In addition, this new set of gene biomarkers, discovered by Health Discovery Corporation, could provide a diagnostic test used to evaluate patients undergoing treatment for BPH.”

Stephen D. Barnhill, M.D., Chairman and Chief Executive Officer of Health Discovery Corporation, commented, "I am very proud of the accomplishments of our scientists in this new biomarker discovery and look forward to beginning the validation and commercialization efforts necessary to create what could be the worlds first non-invasive test for the diagnosis of BPH.”

Detailed information is available on the company web page at www.healthdiscoverycorp.com.

Health Discovery Corporation is a systems biology-oriented biomarker and pathway discovery company, which provides all aspects of First-Phase Biomarker Discovery™. Health Discovery Corporation was established to produce more effective and cost effective diagnostic and drug discovery tools. Founded in September 2003, the Company is headquartered in Savannah, GA.

Market Wire, 8 November 2004

PROSTATE CANCER TREATMENT CAN AFFECT THYROID

Tiny "seeds" containing radioactive iodine are often implanted in the prostate gland to treat cancer. Now, findings from a case report indicate that these seeds can break open and release the iodine, which is then absorbed by the thyroid gland, a key metabolism regulator.

Dr. Qin-Sheng Chen of the Cleveland Clinic Foundation and colleagues describe the patient in a report published in the November issue of the Journal of Urology.

The case patient's thyroid absorption was too low to be clinically important, Chen told Reuters Health. Nevertheless, "since more and more prostate cancer patients will be treated" with this type of treatment, increased rates of thyroid absorption are expected.

Chen and Dr. Henry F. Blair came across this case while performing routine tests to look for seed migration. Since late 2001, a total of 246 patients were evaluated and 23,184 seeds were implanted. Of these, 75 seeds were released in the urine and 25 migrated to the chest.

In the current case, the seeds became damaged in the prostate and released the iodine into the blood. No other occurrences have been identified, but "in cases where the radiation dose to the thyroid is found to be significant, preventive medication -- such as iodine solution -- would be given to minimize possible complications," Chen said. By giving iodine solution, the thyroid gland is less likely to absorb the radioactive iodine released from the damaged seed.

Reuters Health, 26 November 2004

GTI-2040

(Continued from page 1)

Phase II efficacy stage in the above study of GTI-2040 combined with docetaxel in non-small cell lung cancer. The median survival of patients with metastatic prostate cancer is only two to three years, and previously available therapies for HRPC have provided only palliative benefit. Consequently, there is a dire need for new therapies.

The Phase II clinical trial in prostate cancer will establish the efficacy of a combination of GTI-2040, docetaxel and prednisone in HRPC patients with particular attention to the prostate specific antigen (PSA) response.

FDA News Drug Pipeline Alert, 23 November 2004
GREEN TEA
(Continued from page 1)

“GTP also led to increased levels of one of the binding proteins for IGF-1, the insulin growth factor binding protein-3. These observations bear significance in light of studies that indicate increased levels of IGF-1 are associated with increased risk of several cancers, such as prostate, breast, lung and colon.”

GTP modulation of cell growth via the IGF-1 axis coincides with limited production or phosphorylation of key cell survival proteins, including PI3K, Akt and Erk1/2, the research indicated. The PI3K molecular pathway in cells, which includes Akt and Erk1/2, works to promote cell survival, rather than programmed cell death (apoptosis). GTP also caused reduced expression of proteins known to be associated with the metastatic spread of cancer cells. GTP inhibited the levels of urokinase plasminogen activator as well as matrix metalloproteinases 2 and 9, cellular molecules linked to the metastasis.

The green tea polyphenols contributed to minimizing tumor development by governing the amount of vascular endothelial growth factor (VEGF) in the serum of the prostate cancer mouse model. The reduction of VEGF may result from GTP-induced suppression of IGF-1 levels. By reducing the amount of VEGF, GTP works to minimize nutrients supporting tumor growth.

Mukhtar’s colleagues included Vaqar Mustafa Adhami, Imtiaz Ahmad Siddiqui, and Nihal Ahmad from the Univ. of Wisconsin; and Sanjay Gupta from Case Western Reserve University. For more information, please contact: Russell Vanderboom, Ph.D. by e-mail at vanderboom@aacr.org

American Association for Cancer Research website, 1 December 2004

ORAL PHENOXODIOL REPORTED TO SLOW DISEASE PROGRESSION IN LATE STAGE PROSTATE CANCER PATIENTS

Marshall Edwards, Inc., released the final results of a small-scale clinical study of the investigational anti-cancer drug, phenoxodiol, in patients with hormone-refractory prostate cancer (HRPC). The results, presented on the evening of November 19 to the American Association of Cancer Research (AACR) conference on Basic, Translational and Clinical Advances in Prostate Cancer, held in Bonita Springs, Florida, showed that phenoxodiol has a potent ability to slow down the rate of cancer progression as evidenced by PSA levels and clinical status.

Phenoxodiol (oral dosage formulation) is being developed as a treatment for HRPC, both as a first-line chemotherapy, and as a second-line chemotherapy for patients who have failed to respond to docetaxel.

Phenoxodiol is an investigational drug and has not been approved for marketing by FDA. Under U.S. law, a new drug cannot be marketed until it has been investigated in clinical trials and approved by the FDA as being safe and effective for the intended use.

The clinical study was conducted in two Australian hospitals. Nineteen men with HRPC were treated with phenoxodiol daily for 3 weeks each month for 6 months. All men had advanced, metastatic disease, and entered the trial with rising PSA levels. The primary objectives of the study were to examine (a) the safety and tolerability of phenoxodiol in men with HRPC, (b) the ability to maintain a steady-state of phenoxodiol in the blood, and (c) the effect of phenoxodiol on PSA levels and disease progression. The main purpose of the study was to show clinical benefit thereby justifying a large-scale study to determine whether phenoxodiol can reduce tumor progression. Another purpose was to determine an appropriate dosage of phenoxodiol to be used in such a study.

Patients received one of four different dosages of phenoxodiol – 20, 80, 200 or 400 mg each 8 hours for 6 months or until disease progression. Patients considered to have derived a clinical benefit from phenoxodiol after 6 months continued on 200 mg phenoxodiol until disease progression.

Phenoxodiol produced a dose-response effect in terms of disease progression and PSA levels, with the 20 mg dose producing no discernible effect, the 80 mg dose an intermediate effect, and the 200 and 400 mg doses producing a marked effect.

Increasing doses of phenoxodiol resulted in a progressive and marked increase in the time taken for the disease to progress. In the 20 and 80 mg dose groups, all patients had shown disease progression by the end of the study, with average times to progression of 10 and 17 weeks, respectively. However, in the 200 and 400 mg dose groups, 2 of 4 and 3 of 4 patients respectively had no evidence of disease progression at 6 months. PSA levels in 5 patients without disease progression at 6 months were at or below baseline levels.

Two of four patients in the 200 mg dose group, and 3 of 4 patients in the 400 mg dose group showed a PSA response, which taken together with the disease progression data suggests that phenoxodiol monotherapy is exerting a significant anti-tumor effect.

Phenoxodiol was well tolerated in all patients, with no toxicities being reported, including at dosages of 400 mg administered for 6 months, followed by 200 mg for up
to a further 18 months.

Professor Graham Kelly PhD, Chairman, Marshall Edwards, Inc., who presented the data at the conference on behalf of the investigators, said, “These results give us optimism that with phenoxodiol we can slow the rate of tumor progression to the point where we can make a real difference to the survival of men with such advanced cancer. Current therapies offer only modest extensions of life to about half of patients with HRPC, but at the cost of significant toxicity to most men receiving the treatment. Our aim with phenoxodiol is to deliver meaningful prolongation of life in a significant number of patients, with little or no toxicity.”

A Phase IIb/IIa multi-center, international, clinical trial known as the COMPACT (Comparison of Phenoxodiol Against Conventional Therapy) Study in men with HRPC using a phenoxodiol dosage of 400 mg currently is being established. Phenoxodiol is an investigational product that regulates signal transduction pathways in cancer cells resulting in the break down of the intra-cellular proteins - XIAP (X-linked Inhibitor of Apoptosis Protein) and FLIP (Fas Ligand Inhibitory Protein) - which block the ability of the cancer cell to undergo apoptosis via the death receptor mechanism. While these proteins play a vital role in preventing unintentional cell death in healthy cells, they are over-expressed in many forms of cancer, as well as being associated with the development of resistance to anti-cancer drugs.

Phenoxodiol is an investigational drug (is not approved in the US).

More information on phenoxodiol and on the Novogen group of companies can be found at www.marshalledwardsinc.com and www.novogen.com.

Marshall Edwards website
22 November 2004

AIM-PC TRIAL
EVALUATES A NEW
RESEARCH DRUG FOR
METASTATIC AIPC

MedImmune, Inc., a biotechnology firm based in Gaithersburg, MD, is currently sponsoring a phase II clinical research trial—“Androgen Independent Metastatic Prostate Cancer (AIM-PC) Trial”—to evaluate a possible new approach to stopping the progression of prostate cancer and reducing bone loss that may follow treatment. The researchers will evaluate the anti-tumor activity of the investigational drug, Vitaxin®, when added to zoledronic acid plus the current FDA-approved chemotherapy regimen for men with metastatic, androgen independent prostate cancer: docetaxel and prednisone. This randomized open-label clinical trial is being conducted at medical sites throughout the U.S. and other countries.

In men with metastatic prostate cancer that has progressed despite hormone therapy, currently approved treatments cannot cure it and long-term survival rates remain low. Clinical trials are not right for everyone, but they are an important option to understand and consider.

If you have prostate cancer that has progressed after starting androgen deprivation therapy, which includes prior orchectomy or medications that lower your testosterone level, and you are interested in learning more about the AIM-PC clinical trial, please visit the Web site at www.aim-pc.com or call 1-866-289-1385.

If you are interested in having a physician who is conducting the AIM-PC trial speak to a support group in your area, please call 1-866-289-1359.

Matthews Media Group
17 December 2004

PROSTATE CANCER CARE IMPROVES IN THE UK

Men in England who have prostate cancer are being seen quicker and receiving better care, a government report shows.

It examines the progress made in the management of the disease since the NHS Prostate Cancer Programme was introduced four years ago.

Around 98% of men with suspected prostate cancer see a consultant within two weeks of an urgent referral by a GP, compared to 40% in 1997. Prostate cancer campaigners welcomed the report but called for more action.

Dr Chris Parker, of the Prostate Cancer Charter for Action, said: "Prostate cancer is a big killer and it is right we continue to make tackling prostate cancer our priority. "Although there has been encouraging progress on tackling prostate cancer there is still a lot to do".

The NHS Prostate Cancer Programme was the first of its kind, and aimed to focus attention on the most commonly diagnosed cancer in men in England and the second biggest cancer killer in men.

Prostate cancer is the only cancer with a government spending target for research - the target of £4.2 million was reached in 2003/04.

In addition, the number of consultant urologists has increased by 40% - to a total of 503 consultants now compared to 343 in 1997.

Pioneering techniques

Launching the report, Health Minister, Lord Warner said: "We take prostate cancer very seriously.

"That is why four years ago we published the programme to give prostate cancer the priority it deserves.

"As a result a lot of excellent pro-
UK Prostate Cancer
(Continued from page 5)

progress has been made. Patients are being seen more quickly and are getting better care."
He added: "Making sure patients have access to the latest treatments is key to reducing the suffering caused by this condition - that is why prostate cancer is the only to have a specific target for government spending on research.
"This will help to ensure that patients get the benefit of pioneering new techniques like high intensity focused ultrasound for which clinical trials are due to begin early next year."
John Neate, chief executive of The Prostate Cancer Charity, said: "The government's report provides an essential round-up of advances made across the board over the past four years in prostate cancer research, NHS services and information.
"It will form an important baseline for evaluating future improvements." But he added: "We are still in the foothills of the battle against prostate cancer, with a mountain still to climb.
"We need to see a continuing revolution in our approach to this major disease - with increased investment in professional staff, strengthened NHS team working, 'male friendly' primary care services and focused research to secure improved prostate cancer testing and treatments."
BBC News, 9 November 2004
http://news.bbc.co.uk/go/pr/fr/-/1/hi/health/3995377.stm

NIH Study to Compare Prostate Surgery and Drugs
The Minimally Invasive Surgical Therapies (MIST) Consortium for Benign Prostatic Hyperplasia (BPH) has launched a new study to compare long-term benefits and risks of transurethral needle ablation (TUNA) and transurethral microwave thermotherapy (TUMT) to a regimen of the alpha-1 inhibitor alfuzosin and the 5-alpha reductase inhibitor finasteride. The National Institute of Diabetes and Digestive and Kidney Diseases at NIH, part of the Department of Health and Human Services, is investing more than $15 million in the study.
TUNA and TUMT use heat to destroy part of the enlarged prostate to improve urine flow and symptoms. Early studies suggest that these procedures reduce the occurrence of erection or bladder control side effects, which occur more often with the traditional surgery for BPH, known as transurethral resection of the prostate (TURP).
TUNA and TUMT are said to be minimally invasive in part because they typically are done with local anesthesia and men go home the same day, whereas TURP requires general anesthesia and an overnight hospital stay. As for drug therapy, a recently published large randomized study showed that a regimen of finasteride (Proscar) and the alpha-1 inhibitor doxazosin (Cardura) prevents progression of BPH in a significant percentage of symptomatic men and it helps men at high risk avoid surgery.
"It’s easy to see why drug therapy, TUNA and TUMT have been embraced by many urologists and patients,” said Leroy M. Nyberg Jr., Ph.D., M.D., director of NIDDK’s urology trials. “Yet, we don’t know which treatment is more effective in the long run and, for the most part, who would be better served by the drug combination versus one of the minimally invasive therapies.”
By July 2006, researchers plan to have recruited and randomly assigned more than 700 men with moderate to severe symptoms and no prior prostate surgery to one of the three MIST therapies. The men, age 50 and over, will be followed closely for 3 to 5 years, to see who after treatment develops urinary retention, urinary tract infection or unacceptable incontinence; requires more treatment; and failure to improve symptomatically by at least 30 percent.
In 2000, BPH accounted for about 8 million office visits, 117,000 trips to emergency rooms, 105,000 hospital stays and 87,400 TURPs. BPH also cost patients and insurers about $1.1 billion, without considering nutritional supplements and 2.2 million prescriptions, according to NIDDK’s Urologic Diseases in America interim compendium, released this spring.
MIST will also compare TUNA to TUMT and seeks to identify men best suited for each of the three therapies. Changes in sexual function, ejaculation, bladder changes, PSA, prostate size and shape, and ratio of various prostate tissues; and pain before, during and after surgery, among other parameters, will be tracked in search of characteristics predicting likely outcome and effectiveness of therapies.
“Having a protocol to fit the man to the therapy without having to try each treatment along the way should translate into lower costs and more-satisfied patients,” said John W. Kusek, Ph.D., a clinical trials expert at NIDDK.
MIST therapies are approved by FDA, but relative benefits, risks and cost were never compared. Further, there have been few rigorously conducted randomized trials of the minimally invasive surgical approaches. “Previous studies of TUMT and TUNA haven’t looked at side-effects and symptom relief long-term but, after we’ve finished MIST, men and their doctors should be a lot smarter about the options,” said Kusek.
Vidyya Medical News Service
18 November 2004
US TOO ANNOUNCES NEW PROSTATE CANCER PATIENT’S GUIDE TO HORMONAL THERAPY

As part of our continuing mission to provide strong, patient-focused, educational content and information, Us TOO is producing a Prostate Cancer Patient’s Guide to Hormonal Therapy, which will be available on Us TOO’s Web site (www.ustoo.org) in January and distributed to the chapters early next year. Hormonal therapy is being used to treat more men at earlier stages of prostate cancer than ever before. The brochure will describe hormonal therapy and how it is done, and detail side effects that can occur while taking it.

“Hormonal therapy was usually reserved for the treatment of metastatic prostate cancer. Today, we’re seeing the benefits of using this therapy on localized disease as well. That said, it is important that patients are aware of hormonal therapy’s benefits and potential side effects. This brochure will serve as an excellent resource in helping to educate those individuals,” stated Us TOO Treasurer Greg Bielawski, who has been treated with hormonal therapy.

Funding for the brochure comes from TAP Pharmaceuticals.

EFFECT OF TOMATO OIL ON PRECANCEROUS PROSTATE CHANGES

Lycopene, an antioxidant commonly found in tomatoes and tomato-based products, is commonly perceived to reduce the risk of developing prostate cancer.

A new study at Northwestern University seeks to determine whether natural tomato oil with a high concentration of lycopene may reverse or delay progression of high-grade prostatic intraepithelial neoplasia (HGPIN), a condition in which abnormal cells form within the prostate and which is the strongest risk factor yet identified for the development of prostate cancer.

The study is headed by Peter Gann, M.D., professor of preventive medicine at the Northwestern University Feinberg School of Medicine and a member of the cancer epidemiology and prevention program at The Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Lycopene has been found to have anti-tumor activity in a number of laboratory studies. Also, it has been used in a number of cancer studies in humans (e.g., lung, stomach and prostate cancers) that demonstrated a lower cancer rate in people with a high dietary intake of lycopene.

Research has shown an over 20 percent reduced risk for developing prostate cancer in men who ate more cooked tomato products, such as tomato sauce. Additional studies showed that cooking tomatoes and eating them with oil substantially increases the bioavailability of lycopene.

The National Cancer Institute-sponsored study at Northwestern will use tomato extract (literally, tomato oil) from non-genetically modified tomatoes raised in Israel and specially grown to be high in lycopene content.

Results of the study will be useful for clarifying the mechanisms of action of lycopene in the prostate, for designing phase III clinical studies and, more generally, for determining the chemopreventive potential of this relatively non-toxic dietary compound.

“Prostate cancer is a rational target for chemoprevention because of its high public health burden and relatively slow growth rate,” Gann said.

“Although early surgical treatment of prostate cancer might be effective, it involves substantial discom-
MAYO CLINIC DISCOVERS ONE MECHANISM WHY IMMUNE RESPONSE DIFFERS BETWEEN MEN AND WOMEN

Decreasing testosterone boosts immunity because testosterone helps control T-lymphocytes, the attack cells of the immune system, according to Mayo Clinic-led research in laboratory animals. The findings appear in the Nov. 15 edition of the Journal of Immunology (http://www.jimmunol.org/future/173.10.shtml).

“What we are showing is that testosterone seems to impede immunity,” says Eugene Kwon, M.D., the Mayo Clinic urologist and immunology researcher who led the research team. “However, when testosterone is withdrawn, you get an increased host immune response indicated by the rising numbers of immune cells that are available to participate.”

T-lymphocytes are cells that are vital to controlling the body’s immune response. “T cells,” as they are usually called by scientists, are white blood cells that can fight against tumor cells and infection. Alternatively, T cells can help other immune cells known as “B cells” make antibodies to defend the body against certain bacterial and fungal infections, and possibly against cancer. The research findings may have broad potential applications to public health.

Researchers and physicians have known for years that there is a difference in immunity between men and women -- but they have not known why. The researchers discovered one possible mechanism: The presence of testosterone slows or weakens the response of T-lymphocytes. Delving further to discover the mechanism behind this response, the research team found that without testosterone, the T-cells “turn-on” more quickly. It also is possible that other sex hormones play a similar role because testosterone is just one of the hormones known as androgens.

Dr. Kwon frequently cares for patients with prostate cancer. The current experiment grew out of his experience in the clinic. One of the more common forms of treatment for prostate cancer suppresses the patient’s testosterone levels to increase the patient’s immune attack against cancer. To test the role of testosterone on the immune system in the laboratory, the researchers removed testosterone from male mice.

“They suddenly started growing large numbers of new immune cells,” Dr. Kwon says. “We also demonstrated that if you take a male mouse and treat it with chemotherapy you can prompt the mouse to recover its immune system much more quickly simply by removing androgen.”

When testosterone is removed, the immune cells come back strong and aggressive, ready to attack. Says Dr. Kwon, “They become twitchy, very reactive, and in this state they can, in fact, mediate a strong immune response -- which, as physicians, is just what we want.”

Collaborators include scientists from Roswell Park Cancer Institute, Buffalo, N.Y.; the Tumor Immunity and Tolerance Section of the Laboratory of Molecular Immunoregulation, National Cancer Institute; and Howard Hughes Medical Institute/Memorial Sloan-Kettering Cancer Center.

Mayo Clinic, 5 November 2004

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US TOO PROSTATE CANCER EDUCATION & SUPPORT HOT SHEET JANUARY 2005  P. 8