Newsletter

Prostate Cancer 101, Inc.

http://prostatecancer101.org

December, 2013

The Prostate Cancer Information and Support Group of the Mid-Hudson

# Promising Nanomedicine Advances to Phase II Clinical Trials

**Docetaxel has long been used to treat advanced forms of prostate cancer; now an ingenious targeted drug platform will deliver this chemotherapeutic directly to tumors, allowing higher dosing with fewer side effects.**

October 26, 2013 - Docetaxel is a tried and true FDA-approved chemotherapy drug (trade name Taxotere) that has been used since 2004 to treat men with advanced prostate cancer. The drug is given by IV-infusion. Docetaxel is a front-line chemotherapy treatment for men with metastatic treatment-resistant prostate cancer. Because docetaxel is given systemically (throughout the body) the drug floods the body and affects cells and tissues that are not cancerous, causing unpleasant side effects for some patients. In addition, flooding the body with the drug means only a fraction of drug is delivered where it is actually needed—to tumor cells.

With significant funding from the David H. Koch – Prostate Cancer Foundation Program in Nanotherapeutics, a highly innovative way to deliver docetaxel directly to cancer cells has been developed—a polymeric nanoparticle that delivers docetaxel directly to cancer cells. This targeted drug platform allows higher doses to be administered and reach the tumor with fewer side effects experienced by patients. This nanoparticle platform is known as Medicinal Nanoengineering and is being developed by BIND Therapeutics based in Cambridge Mass. Their nanoparticles are referred to as Accurins. Their lead drug candidate is BIND-014 which is now in Phase II clinical trials in men with metastatic treatment-resistant prostate cancer and non-small cell lung cancer.

BIND-014 has shown the ability to shrink tumor size in heavily pre-treated patients (those who have failed to adequately respond to other anti-cancer treatments) as well as in patients with tumors that were thought to be insensitive to taxane-based chemotherapies such as docetaxel. To date, BIND-014 has been well-tolerated by patients who have received the drug in Phase I clinical studies, with the most notable side effect being transient low white blood cell counts in some patients. There has been no nanoparticle-related toxicity noted in any of the study participants.

## Phase I Clinical Trials BIND-014

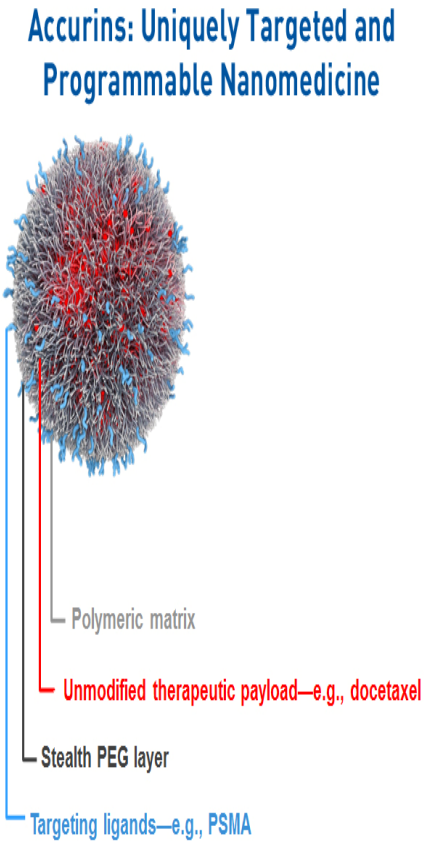
Results of Phase I clinical trials were published last year in *Science Translational Medicine*. That Phase I study established

tolerability of BIND-014 as well as the maximum tolerated dose safe for humans. Updated results of the Phase I study were presented at this year's AACR meeting in Washington, DC by Dr. Daniel Von Hoff. While Phase I studies are generally small and are not designed to fully measure anti-tumor responses, it is encouraging that nine out of 28 patients responded positively to BIND-014. (The study represented a variety of cancer types—a typical Phase I study design.)

Today at the 20th Annual PCF Scientific Retreat, Dr. Christopher Sweeney, Clinical Director, The Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, presented the currently available data on BIND-014. Dr. Sweeney was one of the team members and an author detailing the study results published in *Science Translational Medicine*. He is a consultant for BIND, a publically traded company. Sweeney told of an 80-year-old patient in the Phase I study with advance prostate cancer who, after treatment with BIND-014, experienced a 73% decrease in serum PSA. Sweeney mentioned that the Prostate Cancer Foundation was an early supporter of the basic research behind BIND-014 that helped usher this drug candidate into clinical trials.

## Targeted Nanomedicine

BIND-014 is targeted to an antigen (PSMA) found on the surface of prostate cancer cells and blood vessels in tumors that feed cancer cells.




Think of this nanoparticle technology as a Chemotherapy Express-Line Bus Service that only makes stops at tumor sites where it delivers its therapeutic payload—docetaxel. This limits service only to tumor sites and bypasses healthy tissue along the route, sparing that healthy tissue from damage.

This summer, BIND Therapeutics announced it had begun to give BIND-014 to the first patient in a Phase II clinical trial that will assess the safety and efficacy of this drug in men with metastatic treatment-resistant prostate cancer who have not previously received chemotherapy. The trial will be a 40-patient multi-center study. From more information on this trial go to www.clinicaltrials.gov and enter NCT01812746.

## Primary Outcome Measures of this Phase II study of BIND-014:

- To determine the efficacy of BIND-014 as measured by radiographic progression-free survival (rPFS) in patients with chemotherapy-naïve metastatic CRPC [ Time Frame: Patients will be followed for the duration of treatment, an expected average of 24 weeks ]

  • Number of patients with a progression-free survival of 6 months.

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## • PCF Funding:

The idea to develop aptamer-targeted nanoparticles was first conceived in 2002 and forwarded by the David H. Koch Institute for Integrative Cancer Research at MIT, Brigham and Women's Hospital, the Dana-Farber Cancer Institute, Harvard Medical School and Weill Cornell Medical College. Funding for the research and development program was provided by both public and private sources including the MIT Institute for Integrative Center for Cancer Research, the National Institute for Biomedical Imaging and Bioengineering, a prostate cancer

SPORE Grant awarded to Dana-Farber Cancer Institute, the National Cancer Institute, the NCI Alliance in Nanotechnology and the Prostate Cancer Foundation.
The PCF has heavily funded early work on the development of BIND-014 as well as research on PSMA.
Dr. Sweeney is the principal investigator on the ICECaP Initiative. The Intermediate Clinical Endpoints in Cancer of the Prostate (ICECaP) Working Group is a multidisciplinary team of academic cancer researchers with an interest in prostate cancer and advocates who are joining forces to improve the efficiency of adjuvant clinical trials for prostate cancer in an effort to move potentially life-saving treatments into standard practice sooner.
*Source: PCF(Prostate Cancer Foundation)*

Merry Christmas to All

# Number of Circulating Tumor Cells May Predict Survival in Men with Metastatic Treatment-Resistant Prostate Cancer; May Aid Delivery of Personalized Cancer Care

## Enumeration of Circulating Tumor Cells for Clinical Decision Making

**Howard Scher, MD**
*Memorial Sloan-Kettering Cancer Center, New York*

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**Ongoing Phase III study results of men with advanced form of prostate cancer demonstrates that patients with higher levels of circulating tumor cells and an enzyme marker of disease states in their blood had lower probability of survival at two years. This finding may help doctors determine early on the best course of treatment or enable treatment correction based on CTC levels.**

November 26, 2013 - As their name implies, circulating tumor cells (CTCs) are cancer cells that have detached from a tumor and entered a patient's bloodstream. Circulating tumor cells are a necessary but not sufficient step in the spread of cancer to sites throughout the body to form metastases. Recent technological advances have made it possible to capture these rare CTCs from a patient with a simple blood draw. A goal is for CTCs to be used as a "liquid biopsy" of a patient's cancer to enable physicians to select treatment on the basis of the biology of an individual's disease. Prior research has shown that in men with treatment-resistant prostate cancer who are starting a new chemotherapy regimen, that the number of CTCs in a patient's bloodstream at the start of treatment and following treatment is prognostic for survival and more significant than pre- and post-therapy changes in PSA. Characterizing CTCs at the molecular level can also determine what genetic alterations are present. This knowledge will help researchers to understand why some tumors respond and others do not, or what changes have occurred when a patient fails a specific form of treatment. This type of information is essential to enable the practice of personalized, precision cancer treatment.

Collection and characterization of CTCs remains an emerging technology and science. Study results are needed to demonstrate how the measurement of the number of CTCs and/or the biologic profiling of CTCs can

best inform medical decisions. A critical unmet need in prostate cancer drug development is for post-treatment surrogate endpoints for overall survival that can be used in regulatory filings for drug approvals, and for the individual patient to show that a treatment is working. In a presentation at the Prostate Cancer Foundation's 20th Annual Scientific Retreat in Maryland last month by PCF-funded Dr. Howard Scher of Memorial Sloan-Kettering Cancer Center—reporting on an ongoing study of men enrolled in the Phase III registration trial of abiraterone acetate plus placebo (COU-AA-301)—the data showed that a post-treatment CTC biomarker panel that included the number of cells detected using the CellSearch® Assay (Veridex) in combination with lactate dehydrogenase (LDH) at 12 weeks of treatment met the Prentice criteria as a surrogate for survival. LDH is an enzyme involved in energy production and which is elevated in many disease states.

The study is part of a formal collaboration with the Center for Devices and Radiologic Health (CDRH) branch of the FDA to qualify a surrogate for survival. Dr. Scher is leading the study.
Men in the study, all with treatment-resistant prostate cancer that have previously been treated with chemotherapy (docetaxel), were part of the multinational randomized, double-blind, placebo-controlled study. All men received prednisone. In one arm of the study men received abiraterone acetate (Zytiga), a Cyp17 inhibitor that lowers androgen levels in the testis, adrenal gland and in the tumor itself. Men in the other arm received placebo. Men had CTC counts determined at start of therapy, and four, eight and 12 weeks into therapy. Men with CTC counts of greater than or equal to 5 and LDH levels of greater than 250 IU/L had a lower probability of surviving for two years than men with lower CTC counts and lower levels of the LDH enzyme. A higher rate of men in the treatment arm of the study (those who received both prednisone + Zytiga) had lower CTC counts and lower LDH levels at the 12 week mark. For men with the lowest CTC counts, the probability for two year survival approached 50%. Men with the highest levels of CTCs along with high levels of LDH had less than a 10% probability of reaching the two year mark.
Scher said that demonstrating individual patient level surrogacy in this trial is an important milestone. Validation of the findings using data from other completed and ongoing trials that enrolled men with post-chemotherapy treated CRPC is planned. The results suggest that other treatments be considered for men who have high CTC and LDH levels at week 12.

**PCF Funding:** Dr. Scher is a member of the PCF Scientific Advisory Board and a primary investigator on a 2011 PCF Challenge Award: *Development of Combined Inhibition of AR and PI3K Signaling as a Therapeutic Strategy for Advanced Prostate Cancer.*
*Source: Prostate Cancer Foundation*

**Attention – Business Owners**

We'd like to compile a listing of those who own businesses, so that our members can be aware and utilize your establishment or service. We all know Frank Guido, of Mariner's Harbor, Little Italy and Port of Call fame, who has been so generous to us. So, if you would like to be included in our list please send me information on your business – name, address, phone and a bit of description, so I can work on it for the next newsletter. There's nothing like helping each other out, which is the reason PCa 101 exists. Email or snail mail – it's up to you.

Diane Sutkowski

dsutkowski@hvc.rr.com

# The Prostate Cancer Foundation Unveils Major Initiative to Improve Accuracy of Laboratory Cancer Studies
# Best Practices in Cell Line Authentication

**Howard Soule, PhD**
*Executive Vice President and Chief Science Officer, PCF*

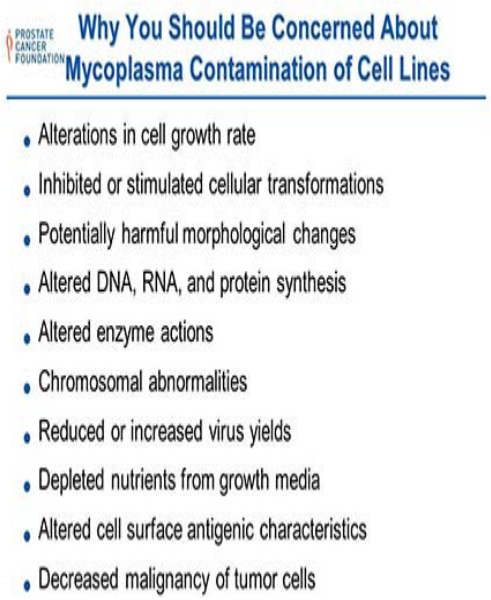
November 21, 2013 - A cell line is a permanently maintained culture of cells in the laboratory that is used to conduct experiments. Cell lines are commonly used to study cancer. Cancer cell lines date back to the 1950s, when the first line was established from a woman, Henrietta Lacks, with cervical cancer. In the decades since, approximately 1,000 cancer cell lines have become essential tools to study cancer cell biology and to test drugs. Indeed, almost every anticancer drug now in use gained early traction through testing on cancer cell lines.[1]

Prostate cancer cell lines are very important tools in the fight

against this disease. However, there are problems with cell lines that need to be addressed. A study published in the *Proceedings of the National Academy of Sciences* in 2011 that looked at 60 established cancer cell lines found that the cell lines studied more closely resembled other cell lines than the cancer type they were supposed to model.[1,2] Another study from the *Journal of Endocrinology and Metabolism* used genetic analysis techniques (short tandem repeat analysis and single nucleotide polymorphism array analysis) to evaluate 40 thyroid cancer-derived cell lines that had been widely used to study thyroid cancer for 20 years.[3] The researchers found the thyroid cell lines to be contaminated with colon and skin cancer cells—only 23 of the 40 lines studied proved to be "pure" for their unique cell line characteristic.

## Cell Line Misidentification a Widespread Problem in Labs

The problem of contaminated cancer cell lines is widespread. Over one-third of human cell lines used for biomedical research are either misidentified or contaminated.[3] Adding to the problem: About one-third of continuous cell line cultures in academic institutions are contaminated with a bacteria known as mycoplasma.[4] Such contamination can affect study results. Soule pointed to a list of ten serious consequences of cell line contamination with mycoplasma bacteria.




*Source*: Pall Corporation
www.pall.com/main/laboratory/literature-library-details.page?id=37153

The Prostate Cancer Foundation (PCF) has put out a mission statement to help resolve this problem, and at the 20th Annual Scientific Retreat Dr. Soule gave a presentation outlining this mission statement. The Prostate Can-

cer Foundation has undertaken a **Cell Line Authentication Initiative (CLAI)**. This calls for widespread implementation of best practices for cell line authentication. Today rapid and accurate DNA profiling techniques such as those mentioned above are available, and when used to verify cell line integrity provide a solution to the problem of misidentified and contamination.[5] Scientists writing in the *Journal of the National Cancer Institute* this year said: Cancer cell lines have been marked by both success and failure. Cell line misidentification arose as the first problem, which should now be minimized by the launch of a standardized protocol for the authentication of human cell lines using short tandem repeat profiling.[6]


Everything was going along fine until they discovered their HeLa cell line expressed Y chromosome markers.

Cartoon by Ed Himelblau, 2011

Editor's note: Folks this cartoon should bring back memories or high-school biology when you learned that only males carry a Y chromosome. As we mentioned, the HeLa cancer cell line was derived from Ms. Henrietta Lacks. No wonder these researchers are having an Uh-Oh moment!

# The Prostate Cancer Cell Line Authentication Initiative

Dr. Soule said the mission of the PCF Cell Line Authentication Initiative (CLAI) is four pronged. First, the CLAI will raise awareness of the issue of cell line misidentification and pathogen contamination and how cell line impurity can affect research outcomes.

Second, the Prostate Cancer Foundation will determine the extent of cell line misidentification and pathogen contamination of human cell lines used by PCF-funded researchers. To accomplish this, all cell lines with be genetically analyzed and compared to database from the American Type Culture Collection (ATCC), a non-profit organization devoted to characterizing biological samples such as cell lines. In addition, genetic testing for the presence of mycoplasma in cell lines will be done. All future research funded by the PCF will require ongoing adherence to these best practices.

Third, PCF will help build awareness of the impact of not implementing ongoing, routine cell line authentication in laboratories that use cell lines.

Fourth, PCF will encourage scientific journals and funding agencies to require CLAI and pathogen testing for mycoplasma and other relevant infectious organisms. While many journals and funding agencies have strongly recommended that cell lines undergo authentication, the scientific field as a whole has not yet implemented cell line authentication best practices.

During his presentation, Soule announced that DNA Diagnostics Center in Cincinnati, a company that does paternity testing and other genetic analysis would offer to PCF investigators (for free!) five cell line authentications per investigator, up to a total of 1,000 tests. Researchers can go to www.ddcmedical.com/pcf for more information on this offer.

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*Source: Prostate Cancer Foundation*


# Researchers Identify Cell Type That May Be Early Inducer of Prostate Cancer

**Work funded by the Prostate Cancer Foundation shows that cells from normal prostate tissue that are low in the AR protein may set the stage for tumor formation; gene signature determined that may aid in drug development, predicting prognosis and perhaps even disease prevention.**

**<u>From the 20th Annual Prostate Cancer Foundation Scientific Retreat in Maryland:</u> Game Changing Research: PCF High-Achieving Young Investigators**
**Andrew Goldstein, PhD**
*University of California, Los Angeles*

November 15, 2013 - Dr. Goldstein's research centers on investigating the cells that are most responsible for tumor regrowth and investigating which cells originate prostate cancer. Last month at the 20th Annual Prostate Cancer Foundation's Scientific Retreat, Dr. Goldstein presented intriguing data on a subset of cells that are associated with inflammation and poor prognosis in prostate cancer.
Prior work has shown that a subset of cells known as $PSA^{-/lo}$ cells that make low or no PSA protein behave in ways that can power prostate cancer progression. This subset of cells express high levels of stem cell (or progenitor cell) genes, which are thought to be very important to tumor recurrence after treatment.

PCF-Young Investigator Andrew Goldstein

Dr. Goldstein reports that he has found that prostate cells from the luminal layer of a normal prostate that are low in the androgen receptor protein ($AR^{low}$ cells) are associated with inflammation and poor prognosis in prostate cancer. (The androgen receptor binds male hormones and regulates many genes. The AR protein can also function as a key driver of prostate cancer.)

The normal prostate is composed of epithelial tissue that is either basal epithelial cells or luminal epithelial cells. Within this population of cells are stem/progenitor cells that give rise to adult prostate epithelial tissue. To date, in human tissue studies, researchers have only identified basal stem/progenitor cells.

But in mice studies, researchers have found stem/progenitor cells in the luminal layer of nor-

mal prostate epithelium. "We went looking for a stem or progenitor cell within the luminal layer of the human prostate, presuming it would likely be relevant for cancer," said Goldstein.

Based on prior scientific clues, Goldstein and colleagues predicted that luminal cells with low expression of the androgen receptor protein might be precursor (progenitor) cells to mature luminal epithelium.
After devising a way to find and isolate prostate luminal cells that lack androgen receptor signaling, they have determined that (similar to $PSA^{-/lo}$ cells) $AR^{low}$ cells behave as progenitor cells.

In addition they've determined that $AR^{low}$ luminal cells sit close to immune signaling cells known as CD45+ cells. "We then hypothesized that inflammation in the prostate might lead to immune system signaling that would cause $AR^{low}$ luminal cells to expand in number and potentially pave the way for a cancer to form if other conditions in the body are also ripe for tumor development.

The researchers then determined a gene signature for $AR^{low}/PSA^{low}$ luminal prostate cells in men with prostate cancer predicted a poor prognosis. "This means that when tumors look more like progenitor cells, patients harboring those tumors have worse outcomes," says Goldstein.

Finally, Goldstein said that in laboratory studies, after mouse castration to deplete androgens, or the addition of a naturally occurring chemical involved in the immune reaction (TNF alpha), the population of prostate luminal progenitor cells increased substantially.

Goldstein says they believe that, taken together, this means that luminal progenitor cells hold important clues about both the origination of prostate cancer and later progression, especially when environmental factors are also taken into account
They plan to further explore whether luminal cells act as progenitor cells only in response to inflammatory processes.

Dr. Goldstein is a 2011 Todd Boehly – Prostate Cancer Foundation Young Investigator.
*Source: Prostate Cancer Foundation*

## Thank you all for your Contributions

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# Does your diet really help prevent prostate cancer?

By Craig Rinder, MD
Updated: 11/15/2013 08:59:51 AM EST

Links between diet and preventing prostate cancer seem to get a lot of media attention. Newspapers frequently run articles about new studies claiming that specific foods, beverages or supplements prevent or slow the advance of prostate cancer. When visiting websites of very reputable institutions like Johns Hopkins or the Mayo Clinic, you'll find long lists of certain foods you should eat or avoid in the name of better prostate health.

The excitement is understandable. Prostate cancer is the most common, non-skin, solid cancer in American men. It is the second leading cause of cancer-related death here in the United States and, in the United Kingdom, it is number one. When you start to read these articles, however, it's amazing to see how little research has actually been done and how many of the findings end up contradicting other studies.

Last year, the Journal of the American Board of Family Medicine published a review of articles linking certain foods and dietary supplements to prostate cancer prevention. The review was conducted by a group of researchers from the University of Montreal who found several hundred examples between 1996 and 2010. The group narrowed their review to 61 articles based on studies involving large numbers of participants. Any article based on studies using animals or that merely made assertions about diet and prostate cancer without clinical research was omitted.

One interesting thing the group found was related to lycopene, a chemical compound that gives tomatoes and other red fruits and vegetables their color. Over the past ten years there has been a lot of interest in lycopene after one study showed that tomato sauce -- though not tomato juice -- was protective against prostate cancer. Later on, a follow-up trial involving thousands of subjects found that lycopene had no effect on preventing prostate cancer or any other type, so it's difficult to draw any definitive conclusions.

In fact, the University of Montreal group did not feel there was enough information to recommend lycopene or any other single dietary element as helpful in preventing prostate cancer. They noted that randomized trials involving vitamin A, vitamin C and multivitamins provided no benefit. Vitamin E and Selenium were two other supplements that showed promise for reducing prostate cancer risk in small studies, but a planned long-term trial involving over 35,000 men found that vitamin E actually increased the risk of prostate cancer in men by 17 percent, while selenium had no benefit and was actually associated with an increased risk of diabetes. The trial was ended early because of these findings.

These examples are an important lesson for anyone who puts too much emphasis on a single dietary element or supplement resulting from one study. No matter how dramatic the results seem to be, they have to be confirmed in large trials in order to become widely recommended.

Most clinicians will recommend a generally healthy diet because we know there is a higher incidence of prostate cancer in countries that have higher fat in their diets, like the United States. This only applies to clinically-diagnosed prostate cancer, however. If you were to biopsy the prostate of men who died from other causes anywhere in the world, the rate of microscopic prostate cancer is the same. That suggests your dietary choices don't protect you from getting prostate cancer, but they can slow the progress to the point where it can be better detected before it causes harm.

Just last month at the European Cancer Congress, a group from the University of California at San Francisco presented a paper on a study involving 46,000 men. The

group had examined six specific prostate cancer reduction strategies and healthy lifestyle activities over a period of 25 years: (1) reducing consumption of red meat; (2) increasing tomato consumption, (3) not smoking, (4) exercising regularly, (5) consuming fatty fish, such as salmon, sardines and trout, and (6) having a body-mass index of less than 30, which means not being obese. The group found that men who adopted at least five of these six habits reduced their risk of lethal prostate cancer by 39 percent compared to those who adopted one or none. That strongly suggests that what is considered a heart-healthy lifestyle is also a prostate-healthy lifestyle.

Other recommendations along those lines include getting more of the fat in your diet from plants instead of animals. Olive oil and canola oil are fats that aid both cardiac and prostate health. Soy products, like tofu, are believed to be preventive, though not proven to everyone's satisfaction. Eating more fruits and vegetables in general is probably healthy, as is eating less dairy products.

Coffee has no proven link to lowering the risk of prostate cancer. There is some limited evidence that green tea may be preventive. This is based on a Japanese study showing people who consumed at least 10 cups of green tea every day had a lower risk of prostate cancer risk than people who consumed three cups of green tea. That's a lot of green tea.

That brings us to early detection and screening which, in my view, is very important for preventing prostate cancer. It has been clearly demonstrated that the death rate from prostate cancer in America has declined significantly since early detection became the standard. Men over the age of 40 should see their primary provider regularly and talk with him or her about whether they should be tested for prostate cancer and when that should occur.

***Craig Rinder, MD,*** *is a board-certified urologist and Director of the Men's Health program at Brattleboro Memorial Hospital. He can be reached at 802-254-8222.*

*Source: Prostate Cancer Foundation*

# High cholesterol fuels the growth and spread of breast cancer

DURHAM, N.C. – A byproduct of cholesterol functions like the hormone estrogen to fuel the growth and spread of the most common types of breast cancers, researchers at the Duke Cancer Institute report.
The researchers also found that anti-cholesterol drugs such as statins appear to diminish the effect of this estrogen-like molecule.

Published in the Nov. 29, 2013, edition of the journal *Science*, the findings are early, using mouse models and tumor cells. But the research for the first time explains the link between high cholesterol and breast cancer, especially in post-menopausal women, and suggests that dietary changes or therapies to reduce cholesterol may also offer a simple, accessible way to reduce breast cancer risk.

"A lot of studies have shown a connection between obesity and breast cancer, and specifically that elevated cholesterol is associated with breast cancer risk, but no mechanism has been identified," said senior author Donald McDonnell, Ph.D., chair of the Department of Pharmacology and Cancer Biol-

ogy at Duke. "What we have now found is a molecule – not cholesterol itself, but an abundant metabolite of cholesterol – called 27HC that mimics the hormone estrogen and can independently drive the growth of breast cancer."

The hormone estrogen feeds an estimated 75 percent of all breast cancers. In a key earlier finding from McDonnell's lab, researchers determined that 27-hydroxycholesterol – or 27HC – behaved similarly to estrogen in animals.

For their current work, the researchers set out to determine whether this estrogen activity was sufficient on its own to promote breast cancer growth and metastasis, and whether controlling it would have a converse effect.

Using mouse models that are highly predictive of what occurs in humans, McDonnell and colleagues demonstrated the direct involvement of 27HC in breast tumor growth, as well as the aggressiveness of the cancer to spread to other organs. They also noted that the activity of this cholesterol metabolite was inhibited when the animals were treated with antiestrogens or when supplementation of 27HC was stopped.

The studies were substantiated using human breast cancer tissue. An additional finding in the human tissue showed a direct correlation between the aggressiveness of the tumor and an abundance of the enzyme that makes the 27HC molecule. They also noted that 27HC could be made in other places in the body and transported to the tumor.

"The worse the tumors, the more they have of the enzyme," said lead author Erik Nelson, Ph.D., a post-doctoral associate at Duke. Nelson said gene expression studies revealed a potential association between 27HC exposure and the development of resistance to the antiestrogen tamoxifen. Their data also highlights how increased 27HC may reduce the effectiveness of aromatase inhibitors, which are among the most commonly used breast cancer therapeutics.

"This is a very significant finding," McDonnell said. "Human breast tumors, because they express this enzyme to make 27HC, are making an estrogen-like molecule that can promote the growth of the tumor. In essence, the tumors have developed a mechanism to use a different source of fuel."

McDonnell said the findings suggest there may be a simple way to reduce the risk of breast cancer by keeping cholesterol in check, either with statins or a healthy diet. Additionally, for women who have breast cancer and high cholesterol, taking statins may delay or prevent resistance to endocrine therapies such as tamoxifen or aromatase inhibitors.

The next steps for research include clinical studies to verify those potential outcomes, as well as studies to determine if 27HC plays a role in other cancers, McDonnell said.

###

In addition to McDonnell and Nelson, study authors include Suzanne E. Wardell, Jeff S. Jasper, Sunghee Park, Sunil Suchindran, Matthew K. Howe, Nicole J. Carver, Ruchita V. Pillai, Patrick M. Sullivan, Varun Sondhi, Michihisa Umetani and Joseph Geradts.

The National Institutes of Health (K99CA172357)
(R37DK048807) and the Department of Defense funded the study.

*Source: Medical Breakthroughs by Ivanhoe*

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**Prostate Cancer 101, Inc.**
**8 Alcazar Avenue**
**Kingston, NY 12401-4302**

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**Contact**
Paul Totta 845 297-7992
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**If you need or want to help:**

***PCa 101 Seminar***
***First Tuesday of every month***

Fred Bell 845 338-1161
Fwbelljr1@aol.com

Gene Groelle 338-1805
Gro226@aol.com

***Website & Newsletters***
http://prostatecancer101.org
Walt Sutkowski 331-7241
wsutkowski@hvc.rr.com

***Greeters/Church Hall Setup***
Bob Miggins 382-1305
GD7M37@verizon.net

***Programs***
Arlene Ryan 338-9229
Aryan@hvc.rr.com

Diane Sutkowski 331-7241
dsutkowski@hvc.rr.com

***Membership & Administration***
Diane Sutkowski 331-7241
dsutkowski@hvc.rr.com