

Immunotherapy Offers Hope For Some Men With Aggressive Prostate Cancer

New research published today in the Journal of Clinical Investigation, led by scientists at the Institute of Cancer Research in the U.K. and Dana-Farber Cancer Institute in Boston, suggests that men with specific DNA defects in their prostate cancers may respond especially well to immunotherapy agents.

“Our study found that some men with advanced prostate cancers have genomic mutations in their tumors that make the disease unstable, aggressive

and resistant to standard therapies,” said Professor Johann de Bono, Director of the Drug Development Unit at the Institute of Cancer Research and the lead author of the study.

These mutations are defects in genes that control a process called DNA mismatch repair. Occasionally, as a result of normal errors in DNA replication or damage by external factors such as carcinogens, DNA bases are arranged in a haphazard way, with DNA letters not arranged opposite their

intended pairs. This is called a mismatch and is often repaired in healthy cells, but in people with defects in their mismatch repair genes, this process is impaired or even absent altogether, meaning that these mismatch mutations progressively accumulate in the cancer cell DNA.

“These men with ‘mismatch’ repair mutations only live about half as long as others who also have advanced

(Continued on page 2)

Medical Advisors

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Thanks!

Next Meeting:

Wednesday, October 17, 2018

Speaker: Gregory Harochaw

Title: “Sexuality After Prostate Cancer”

Location: The First Unitarian Universalist Church of
Winnipeg, 603 Wellington Crescent

Time: 7 – 9 pm.

(First hour for general discussion; second hour for expert guest speaker)

*Free Admission Everyone Welcome
Plenty of free parking Free Light Refreshments*



The Manitoba Prostate Cancer Support Group offers support to prostate cancer patients but does not recommend any particular treatment modalities, medications or physicians ; such decisions should be made in consultation with your doctor.

MPCSG – active since 1992.

Thought of The Day

Knowledge is knowing a tomato is a fruit; Wisdom is not putting it in a fruit salad.

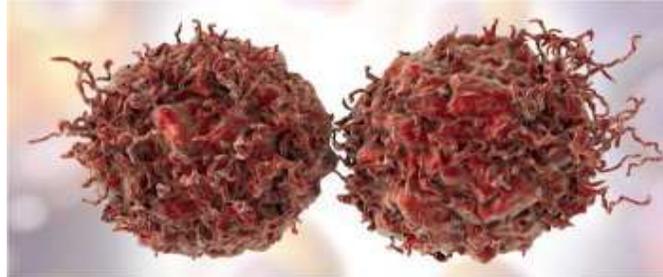
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prostate cancer but whose tumors don't carry such mutations," said de Bono.

DNA mismatch repair defects are common in some types of cancer, notably colorectal cancers, but the new study showed that these defects were also present in 8.1% of men with advanced prostate cancer. The men with DNA mismatch repair mutations in their tumors survived for under four years after diagnosis, compared with seven years for men with advanced prostate cancer with no detectable mismatch repair defects, but the new research suggests that the men with the mismatch repair defects may respond particularly well to immunotherapy agents known as immune checkpoint inhibitors.

"We discovered that tumors with mismatch repair mutations have key hallmarks which make them particularly likely to respond to checkpoint inhibitor immunotherapy," said de Bono.

The researchers looked at the prostate cancer cells from tumor biopsies of 124 men and tested for the levels of a protein called PD-L1, which is essentially a warning light to the immune system, telling it to leave the



Immunotherapy to unleash the immune system against prostate cancer may be a new treatment option for men with specific DNA defects in their cancer cells.

cell alone. High levels of PD-L1 can make cancer cells especially resistant to this immune system monitoring, but treatment with immune checkpoint inhibitors can target this protection, unleashing the immune system on the cancer cell.

The study found that half of all men with mismatch repair defects in their

tumors had high PD-L1 levels, compared to less than 10% of men with normal mismatch repair. The published work builds upon results presented at the American Society for Clinical Oncology meeting in June, which

indicated that DNA mismatch repair defects were responsible for favorable responses to Keytruda, and the scientists are currently running new clinical trials to test the effectiveness of immune checkpoint inhibitors in these patients.

"We are now developing tests that could pick out patients with these mutations, and we're running new clinical trials to see if immunotherapy can offer new hope for these men," said de Bono.

Victoria Forster Sep 4, 2018

source: <https://www.forbes.com/sites/victoriaforster/2018/09/04/immunotherapy-offers-hope-for-some-men-with-aggressive-prostate-cancer/#e7cac4974ed4>

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Single PSA Screening Does Not Improve Prostate Cancer-Related Mortality

Recommendations about population-wide PSA screening are mixed, with some studies suggesting that the potential benefits of early diagnosis are outweighed by overtreatment. A single prostate-specific antigen (PSA) screening may not improve the 10-year rate of prostate cancer-specific survival, though low-risk disease is more likely to be detected, according to research published in *JAMA Oncology*.¹

Recommendations about population-wide PSA screening are mixed, with some studies suggesting that the potential benefits of early diagnosis are outweighed by overtreatment. No major study has, however, determined whether a single PSA screening is likely to

benefit patients over a long follow-up period.

For this study (the Cluster Randomized Trial of PSA Testing for Prostate Cancer; CAP), researchers attempted to "determine the effects of a low-intensity, single invitation PSA test and standardized diagnostic pathway on prostate cancer-specific and all-cause mortality while minimizing overdetection and overtreatment."

Of over 415,000 enrolled patients, 189,366 were randomly assigned to undergo a single PSA test (intervention group) and 219,439 were assigned to a control group. The mean age was 58.5 years vs 58.6 years in the intervention

vs the control group, respectively; 3.6% vs 3.7% of patients had diabetes and 8% vs 7.8% of patients were obese.

Of patients assigned to the intervention group, 64,436 underwent PSA testing and had a valid result. Eleven percent of these patients had a PSA level between 3 ng/mL and 19.9 ng/mL; 85% of patients in this PSA range underwent biopsy.

The median follow-up was 10 years; during this period, 549 patients in the intervention group and 647 patients in the control group died of prostate cancer (rate ratio [RR] for deaths per

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1000 person-years, 0.96; $P = .5$). More patients in the intervention group were, however, diagnosed with prostate cancer during follow-up (8054 vs 7853; RR, 1.19; $P < .001$).

Prostate cancers diagnosed in the intervention group were, furthermore, more likely to have a Gleason grade of 6 or lower.

The rate of all-cause mortality was also similar between the groups: at 10 years,

25,459 patients in the intervention group and 28,306 patients in the control group had died (RR, 0.99; $P = .49$).

The authors concluded that “there was no significant difference in prostate cancer mortality after a median follow-up of 10 years but the detection of low-risk prostate cancer cases increased. Although longer-term follow-up is under way, the findings do not support single PSA testing for population-based screening.”

March 06, 2018

source: <https://www.cancertherapyadvisor.com/prostate-cancer/prostate-cancer-psa-screening-single-no-improved-mortality-outcomes/article/749089/>

Reference

Martin RM, Donovan JL, Turner EL, et al. Effect of a low-intensity PSA-based screening intervention on prostate cancer mortality: the CAP randomized clinical trial. *JAMA Oncol.* 2018 Mar 6. doi: 10.1001/jama.2018.0154 [Epub ahead of print]

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A Great Evening !

On Sept 19 the Caboto Centre in Winnipeg was the venue for the 2018 **September Awareness Evening about Prostate Cancer**. The event was a great success, with more than 180 people, mostly patients but including also family members and other support persons, attending. The highlight speaker, Dr. Darrel Drachenberg, urological oncologist and surgeon at CancerCare Manitoba, delivered a masterful keynote address “*Prostate cancer treatment through the years..... past, present and future*”. This covered the decades long journey beginning with the pioneering early surgical and radiation approaches of the last century to the present menu of sophisticated treatment options, and on to the exciting developments of the future, with personalized medicine based on genetics and immunotherapy just around the corner. (Well, maybe the next corner!) The take home message was that there have been enormous advances

in treating even the difficult cases and that more, much more, exciting progress is underway in research labs and clinics around the world.... truly a welcome message for all patients and their loved ones.

questions and concerns posed by the attendees. Lots of good advice there, along with a few chuckles.

All in all Dr. Drachenberg, both in the keynote address and in the Q&A which followed, gave the audience plenty of food for thought and reason for optimism about the future treatment of this disease. This was truly a great evening. And we're already planning for next year.

P.S.

Prior to the keynote address a few minutes were spent in recognition of our financial sponsors, which include corporate donors, community minded organizations and individual donors. Special recognition was accorded to the Manitoba Ride-For-Dad organization (see photo). Without these sponsors we could not continue to operate.

Thank you to all of them.

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Photo caption: Ride-For-Dad members (Kirk Van Alstyne, Frank Wurr, Liz Southby and Scott Southby) present cheque to MPCSG treasurer Al Petkau (extreme right). The RFD organization has been and continues to be a strong supporter of our activities. Their annual spring motorcycle cavalcade and “get checked” ad campaign does a great service to the prostate cancer community in Manitoba by raising funds and awareness. The latter is especially important in reaching those men who already have prostate cancer, but don't yet know it. Photo credit: Wally Jackson

Following the more or less formal keynote address there was a spirited Q&A session covering a broad range of

Prostate Cancer Canada Launches Latex Glove Campaign to Promote Testing

Prostate Cancer Canada is encouraging men to get tested for the potentially deadly disease with a bold campaign that references historical and fictional characters in the form of latex gloves — yes, those donned by doctors for the often dreaded digital rectal exam meant to detect the presence of tumours in the male sex gland.

Called “Famous Fingers,” the campaign features 13 gloves — index fingers raised — that are hand-painted with iconic designs for such luminaries as Babe Ruth, Napoleon, Winston Churchill and King Tut.

Prostate Cancer Canada is encouraging men to get tested for the potentially deadly disease with a bold campaign that references historical and fictional characters in the form of hand-painted latex gloves.

Each glove is accompanied by the figure’s signature accomplishment. Take, for instance, Sherlock Holmes: “His finger cracked every case. Next up, your prostate?”

“Men may not like inherently to be talking about their prostate, but we do know they like talking about movies and music and sports,” said Yaz Maziar, senior director of marketing and communications for Prostate Cancer Canada (PCC).

“So when you have figures in the campaign like Babe Ruth or Beethoven or Abe Lincoln or Thor or Frankenstein, these are things that men will find humour in,” he said. “And with all the flutter out there to break through that noise, this is helping guys have some fun conversations online around an important health topic.”

All levity aside, Famous Fingers isn’t so much about prodding men to get a digital exam, but to discuss prostate cancer with their doctor and to have a test that measures the level of prostate specific antigen, or PSA, in their blood, said Dr.

Stuart Edmonds, PCC’s vice-president of research, health promotion and survivorship.



Prostate Cancer Canada is encouraging men to get tested for the potentially deadly disease with a bold campaign that references historical and fictional characters in the form of hand-painted latex gloves. (HO / THE CANADIAN PRESS)

An elevated level of PSA can be indicative of cancer in the walnut-sized gland and early detection can make a critical difference in the odds of survival, said Edmonds, noting that prostate cancer causes virtually no symptoms in its early stages.

“And oftentimes when men start to exhibit symptoms of prostate cancer, it’s already late-stage and so the options for treatment are reduced, and actually you’re looking at a very aggressive form of treatment that may lead to men passing away,” he said.

“So the idea is to detect prostate cancer early to be able to intervene, if necessary, early with radiation therapy or ... surgery. And if you can catch it when it’s still localized, the chances for survival are close to 100 per cent. If you don’t catch it early and it’s metastasized, (five-year) survival goes down to around 26, 27 per cent.”

In 2017, an estimated 21,300 Canadian men were diagnosed with prostate cancer and 4,100 died from the disease, says the Canadian Cancer Society. Prostate cancer is the third deadliest malignancy among men after lung and colorectal cancer.

Despite controversy over PSA testing — in some cases, false positives or misinterpretation of results can lead to unnecessary or excessive treatment — Edmonds said Prostate Cancer Canada supports its use and suggests men should start discussing the issue with their doctors when they reach their 40s.

One way to deal with the risk of overtreatment is to put men on “active surveillance,” in which close monitoring with regular PSA testing and possibly biopsies will determine if their tumour has grown and warrants more aggressive treatment.

“What we’ve seen over the last 20 years is a 40 per cent reduction in the mortality rate in Canada from prostate cancer,” said Edmonds, who attributes much of that decline to PSA testing, which was introduced about 25 years ago.

Yet many men are reluctant to raise the subject of testing for prostate cancer with their doctors, in part because it means talking about their urinary and sexual anatomy, he said. Treatment for prostate cancer can lead to urinary incontinence and sexual dysfunction.

“There’s a sense of being fallible, showing weakness, and we’re talking about something that can actually be emasculating.”

The Famous Fingers campaign “is a way of catching people’s attention,” Edmonds said.

“We know that there are issues around men going to get tested or ask

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questions of their physician about prostate cancer and this is a way we can really raise awareness and say it's not a bad thing to have that discussion and it's not a bad thing to get tested either."

However, a professor of marketing at Queen's University's School of Business suggests the campaign could fail to have its intended impact because of its pointed focus on rectal exams, even though it's done in a light-hearted way.

"It's humorous, but frankly what the advertisement will say to the average

man is: 'Why don't you go and get a finger put in your rectum and find out whether or not you have cancer,' " Ken Wong said from Kingston, Ont. "It's really not a message that endears one to the idea of having an examination.

"If their strategy was to increase the pool of people who are willing to be checked for prostate cancer, that's the wrong message to do it with," he said, adding that the use of humour could obscure more critical issues, such as the potential impact of the disease and treatment on the ability to have sex.

"Ask yourself which sells best — sex or humour? Most people would say sex."

By SHERYL UBELACKER

The Canadian Press

Tues., Sept. 11, 2018

source: <https://www.thestar.com/news/canada/2018/09/11/prostate-cancer-canada-launches-latex-glove-campaign-to-promote-testing.html>

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New Study Suggests Routine Testing For Prostate Cancer Could Be Dangerous

The prostate-specific antigen (PSA) test is the only widely used test currently available to screen for prostate cancer.

Washington: Routine testing for prostate cancer is not recommended for most men as the benefit is small and uncertain and it also has a number of harmful effects, suggest experts.

Acknowledging that some men, such as those with a family history of prostate cancer, may be more likely to consider screening, experts suggest that they should have discussions about possible harms and benefits with their doctors.

The prostate-specific antigen (PSA) test is the only widely used test currently

available to screen for prostate cancer. It is used in many countries but remains controversial because it has increased the number of healthy men diagnosed with and treated unnecessarily for harmless tumours.

To explore this further, research methodologists carried out a detailed analysis of the latest evidence using the GRADE approach (a system used to assess the quality of evidence).

Based on a review (more than 700,000 men in clinical trials), which found that if screening reduces prostate cancer deaths at all, the effect is very small, the panel advises against offering routine PSA screening and says most men will decline to screen because of the small

and uncertain benefits and the clear harms.

However, men at higher risk of prostate cancer death (for example, those with a family history of prostate cancer or of African descent) may be more likely to choose PSA screening after discussion of potential benefits and harms of testing with their doctor, authors concluded.

The findings appeared in the Journal of The BMJ.

Sept. 6, 2018

<https://www.deccanchronicle.com/lifestyle/health-and-wellbeing/060918/new-study-suggests-routine-testing-for-prostate-cancer-could-be-danger.html>

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Editorial comment, concerning PSA screening.

The confusing recommendations regarding the value of PSA screening continue, as witnessed by the two studies summarized in this newsletter (see articles beginning on page 2 and 5, respectively). In the first article the conclusion is that such screening is of little value to the general population, since the overall mortality due to prostate cancer is unchanged by the screening. In the second article the conclusion is that such screening is "possibly dangerous" because of over diagnosis and over treatment.

The conclusions as stated are valid but miss the point that both result from the fact that aggressive prostate cancer is rare, so that the benefit of treating those patients who need it is diluted to statistical insignificance in the larger pool of patients where treatment is of no benefit vis-à-vis cancer mortality.

This in no way reduces the significance of early detection and treatment for those patients afflicted with the aggressive form of prostate cancer. For them early detection and treatment can be lifesaving. Unfortunately, there is no way of knowing without the test whether you have early cancer in your prostate, and if you do, whether it is of the dangerous variety.

So what should the average man do in regard to testing? It's really quite simple. Do the PSA test, but do not rush into treatment at the first sign of an elevated test result. Rather, work with your medical specialist(s) to determine whether your cancer is of the aggressive variety which warrants treatment. And of course do not do treatment if it is not needed, thereby avoiding the negative side effects which almost always accompany treatment.

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Hormone Therapy Could Make Prostate Cancer Worse

Scientists at Cedars-Sinai have discovered how prostate cancer can sometimes withstand and outwit a standard hormone therapy, causing the cancer to spread.

Their findings also point to a simple blood test that may help doctors predict when this type of hormone therapy resistance will occur.

Prostate cancer is the second-leading cause of cancer death in men, behind lung cancer, killing nearly 30,000 in the U.S. each year, according to the American Cancer Society.

In its early stages, the most common type, adenocarcinoma, is curable and generally responds well to therapies, including those that target androgen — a male sex hormone that stimulates tumor growth.

However, in certain patients, the cancer becomes resistant to androgen-targeted therapy, and the cancer recurs or spreads.

One possible reason for that resistance, the study indicated, appears to be that the therapy causes some adenocarcinoma cells to become neuroendocrine cancer-type cells — a rare type that normally appears in fewer than 1% of prostate cancer patients.

“This transformation is a problem because neuroendocrine prostate cancer is especially aggressive, metastasizes more readily and is more resistant to both androgen-targeted therapy and chemotherapy,” said Neil Bhowmick, PhD.

He is senior author of the study,

published in the *Journal of Clinical Investigation*, and Rajeev Mishra, PhD, former project scientist in his laboratory, is the lead author.

Bhowmick said about one-fourth of the patients who receive androgen-targeted therapy may relapse with tumors that show features of neuroendocrine prostate cancer and develop treatment-resistant disease, according to published research.



To learn more about this process, the investigators examined how cancer cells interact with the supporting cells near the tumor, referred to as the tumor microenvironment, in laboratory mice.

They found these interactions raised the level of the amino acid glutamine, turning the supporting cells into “factories” that supplied fuel for the cancer cells.

“While glutamine is known to spur cancer growth, its role in prostate cancer cells to trigger reprogramming of adenocarcinoma cells into neuroendocrine cancer cells is a new and important finding,” said Roberta

Gottlieb. Gottlieb was a co-author of the study.

The team also examined how androgen-targeted therapy affected the cancer microenvironment.

“To our surprise, we found this type of therapy further changed the cellular environment in a way that caused adenocarcinoma cells in the prostate to transform into neuroendocrine cancer-type cells,” said Bhowmick, professor of

Medicine and Biomedical Sciences.

As the final step in validating the findings in mice, investigators compared levels of glutamine in the plasma of small groups of patients — one with treatment-responsive prostate cancer and the other with treatment-resistant prostate cancer.

They found that levels of glutamine were higher in the second group.

This finding has potential implications for treating prostate cancer patients.

“The study raises the possibility that a simple blood test measuring glutamine might be able to pinpoint when androgen-targeted therapy is failing in a prostate cancer patient and even predict when therapy resistance will occur,” said Posadas, who co-authored the study.

source: Cedars-Sinai Medical Center

September 6, 2018

<https://knowridge.com/2018/09/hormone-therapy-could-make-prostate-cancer-worse/>

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Prostate Cancer ADT Linked to Higher Risk of Liver Diseases

Development of liver disease is higher in men who undergo androgen deprivation therapy for prostate cancer than in those who do not, a study found.

Men who undergo androgen deprivation therapy (ADT) for prostate cancer (PCa) are at elevated risk of developing non-alcoholic fatty liver disease and other liver diseases, a study found.

Compared with PCa patients who did not receive ADT, those who did had a 54% increased risk of being diagnosed with non-alcoholic fatty liver disease, in analyses that included propensity score adjustment, researchers led by Quoc-Dien Trinh, MD, of Brigham and Women's Hospital in Boston, reported in *The Journal of Urology*.

Using the Surveillance, Epidemiology and End Results (SEER)-Medicare database from 1992 to 2009, he and his colleagues identified 82,938 men aged 66 years or older diagnosed with localized prostate cancer. They excluded from the study men with pre-existing non-alcoholic fatty liver disease, other liver diseases, diabetes, or metabolic syndrome. Overall, 37.5% of patients underwent ADT.

In addition to non-alcoholic liver disease, ADT was associated with a significant 35%, 41%, and 47% increased risk of being diagnosed with liver cirrhosis, liver necrosis, and any liver disease, respectively.



Development of liver disease is higher in men who undergo androgen deprivation therapy for prostate cancer than in those who do not, a study found.

The authors observed a dose-response relationship between the number of ADT doses and non-alcoholic fatty liver disease and any liver disease.

Limitations of the study included its

observational design.

In an editorial accompanying the study by Dr Trinh and his team, Jehonathan H. Pinthus, MD, of McMaster University in Hamilton, commented that the finding that ADT is associated with a greater risk of liver disease, particularly non-alcoholic fatty liver disease, “is an important observation because it highlights a clinically important metabolic perturbation of ADT which is probably unfamiliar to most urologists.”

Reference

Gild P, Cole AP, Krasnova A, et al. Liver disease in men undergoing androgen deprivation therapy for prostate cancer. *J Urol*. 2018;200:573-581.

Pinthus JH. *J Urol*. 2018;200:580

Jody A. Charnow, Editor
September 07, 2018

source: <https://www.renalandrologynews.com/prostate-cancer/prostate-cancer-androgen-deprivation-therapy-ups-risk-of-liver-diseases/article/794203/>

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“You Can Help Spread The Word About Prostate Cancer”

Prostate cancer is one of the most common cancers in men. Discovered early, it can be successfully treated in the majority of cases. Such early discovery is dependent on men being aware of the facts about this disease and getting checked. *Early discovery saves lives.*

To help raise awareness and encourage “getting checked” the Manitoba Prostate Cancer Support Group is happy to provide speakers to make presentations to interested groups in the community. There is no charge for this service and the size of

the group doesn't matter. If you are involved with a group that would like to learn more about prostate cancer, and perhaps save some lives in the process, please contact Pat Feschuk (tel: 204-654-3898; email: lizpat@shaw.ca). *Remember that if a man has prostate cancer the sooner he learns about it the better. Not knowing about it simply allows it to grow and spread. So do something about it help spread the word.*

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- Dec.** NO MEETING
- Jan. 16, 2019** TBA. Watch for it.

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- Irek Iskat — membership
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For general information please contact Jos Borsa at number listed above

All meetings (except September) will be held at :
 The First Unitarian Universalist Church of Winnipeg,
 603 Wellington Crescent

All meetings are 7 – 9 pm.
 (First hour for general discussion;
 second hour for expert guest speaker)

Everyone Welcome Plenty of free parking



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