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Thanks!

Thought of The Day

“All you need is the plan,
the road map, and the
courage to press on to
your destination.”

- Earl Nightingale

Public meetings cancelled until further notice

Covid-19 Update_June 2021

Given the current surge in covid cases here in Manitoba I guess we'll have to be patient for a while longer. However the outlook is not all bad as vaccination is proceeding apace so that in a few more weeks the majority of Manitobans will have been vaccinated. That should bring the epidemic to an end. It is encouraging to note that in jurisdictions where vaccination has been successfully implemented life rapidly returns to normal. We eagerly anticipate reaching that happy condition here in Manitoba. In the meantime stay safe, get vaccinated and encourage your circle of acquaintances to do the same. Hopefully the dawn following this dark night is just around the corner.

The Board

Hopes For New Prostate Cancer Treatment After Breakthrough In Understanding Of Disease's Resistance To Drugs

A new treatment that may extend the lives of thousands of prostate cancer patients could be available within a decade after scientists identified a key cause of the resistance the disease develops to effective drugs.

Prostate cancer treatments work by reducing the level of testosterone and other male hormones the tumours rely on for growth.

However, over two to three years the cancer becomes resistant to the treatment, typically leaving the patient

between 12 months and five years to live.

Now, researchers have identified a protein – known as JMJD6 – that causes the cancer to become resistant to the treatment by reducing its reliance on hormones – although it's not yet understood how the process works.

They are now working to develop a drug that effectively shuts down the activity of the protein, in the hope of prolonging the effectiveness of hormone

reducing therapy and extending the lives of the patients.

They hope to have a drug ready for clinical trials within five years that, if all goes well, would be used on the health service within ten years. However, they strongly caution that it's still early days with far more research needed and no guarantee of success.

But with about 12,000 men in the UK dying from prostate cancer every year,

(Continued on page 2)



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.

(Continued from page 1)

the finding has raised hopes that thousands of people a year could have their lives extended by a new drug – in some cases potentially by years.

“This protein could be a key to preventing resistance to treatment. It may allow us to discover and develop new drugs that could prevent, delay or even reverse resistance to current therapies and help improve the outcome for patients with advanced prostate cancer,” said Adam Sharp, of The Institute of Cancer Research.

Any drug is likely to be used in combination with hormonal therapies such as enzalutamide and abiraterone and taken in the form of a pill.

“These results are highly promising and we hope will inform the development of new treatments to give men with advanced prostate cancer valuable extra time with their loved ones,” added Simon Grieveson, head of research at Prostate Cancer UK, which part funded the research.

Professor Charlotte Bevan, of Imperial College London, who was not involved in the research, said: “The major cause of death in prostate cancer is resistance to existing therapies, and so the holy grail is to find new therapies that can work when others fail. Excitingly, this shows that reducing JDJM6 reduces growth of prostate cancer cells. Targeting JDJM6 therapeutically is definitely an exciting option.”

Michelle Mitchell, chief executive of Cancer Research UK, which also helped fund the study, said “Hormone treatments like abiraterone have extended the lives of thousands of men in the UK. But some cancers stop responding to these types of therapies, so finding newer and better treatments is vital.”

“Although this is early research, it has revealed a new drug target that could become a promising treatment for prostate cancers that are no longer responding to current treatments,” she said.

The research is published in the journal *Cancer Research* and used data from ICR’s canSAR cancer drug discovery database.

Elevated levels of the protein in question – known as JMJD6 – also play a role in ovarian, breast, lung, glioblastoma and colon cancer and so blocking those may also help treat those forms of cancer further down the line.



How existing treatments work

Prostate cancer is treated by starving the cancer of testosterone and other male hormones, or androgens, which it needs to grow and spread. The treatment is known as androgen deprivation therapy.

The hormones trigger the growth of cells by binding to a protein called the androgen receptor and this therapy means these receptors have much less hormone to bind with.

But over time, the JMJD6 protein renders the hormone treatment ineffective.

The researchers found that that the protein has a ‘cavity’ that makes it amenable to small compound binding to potentially block its function – which means they should be able to develop a drug to block it. They also showed that if they produce mutations within that cavity, then JMJD6 is no longer able to function.

Ten years of the canSAR database

Ten years ago, Institute of Cancer Research scientists launched canSAR – the world’s largest database for cancer drug discovery.

It brings biological, chemical, pharmacological and disease data together with machine learning to offer predictions about how proteins and drugs may interact. In other words, canSAR is capable of complex virtual experiments and can spot opportunities for future cancer treatments that no human eye could see.

CanSAR contains records of more than 1.9 million drugs and chemical compounds, 2.8 million gene mutation records from cancer patients, and more than 228,000 clinical trial records – and therefore condenses more data than would be generated by 1 million years of use of the Hubble space telescope.

Since its first release in 2011, canSAR has been accessed by more than 200,000 people from 200 countries, and has been cited in more than 300 research papers.

Tom Bawden 22/05/2021

Source: <https://www.msn.com/en-gb/health/medical/hopes-for-new-prostate-cancer-treatment-after-breakthrough-in-understanding-of-disease-e2-80-99s-resistance-to-drugs/ar-AAKg7g0>

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Combination Immunotherapy For Metastatic Prostate Cancer Shows Promise

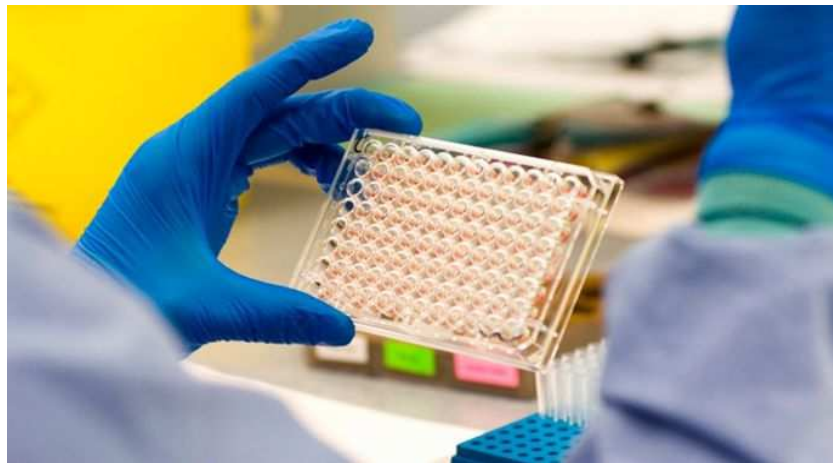
A combination of two antibody therapeutics - nivolumab and ipilimumab - has achieved the best response yet seen in the treatment of metastatic prostate cancer, according to early results from a UCL-led Phase II trial.

Prostate cancer is the second most common cancer affecting men globally and the fourth most common cancer overall. Many patients with prostate cancer do not require treatment or are successfully treated, but a proportion will experience spread to other organs, which is called metastatic prostate cancer. Metastatic prostate cancer can be controlled with hormone therapy but invariably this stops working, a state known as metastatic castration-resistant prostate cancer' (mCRPC). Despite recent advances in treatments for mCRPC the disease is incurable and has a prognosis of only 2-3 years.

The ongoing phase II NEPTUNES trial is exploring whether treatments that boost the body's immune system (called checkpoint inhibitors) can provide benefit for patients with mCRPC. In April 2021, Dr Mark Linch from the UCL Cancer Institute, principal investigator of the NEPTUNES trial, presented preliminary data from the trial at the American Association for Cancer Research (AACR) virtual annual meeting.

Checkpoint inhibitors (CPIs) have demonstrated deep and durable responses for a range of cancers but there has been limited success in prostate cancer so far. This may be

because prostate cancers are difficult for the immune system to see and hard to access due to chemical and physical barriers around the tumour. The NEPTUNES trial is testing whether a subgroup of patients which have either certain defects in the mechanism of DNA repair (making them more visible to the immune system) or already have immune cells within the tumour may render them particularly sensitive to these treatments. This combination of features has been coined the immunogenic signature (ImS+).



Nivolumab and ipilimumab are given for up to four cycles together, with nivolumab alone then used for up to a year after a 6-week gap. Cancer induces an unwanted break mechanism on the cancer killing T-cells (immune cell) enabling further cancer growth. This break can be blocked with CPIs activating the T-cells, which hopefully then find, kill and keep remembering to kill the cancer. Nivolumab blocks the PD-1 break and ipilimumab blocks the CTLA-4 break. Initial data on 35 patients with the appropriate immunogenic signature showed that 10 patients achieved the pre-specified set of criteria for a positive response (28.6% response rate). Although the data do not yet provide definitive evidence of a treatment effect, this is the highest response rate yet for

immunotherapy in mCRPC and several of the responding patients have had a durable response.

“These are the best results we've seen with this kind of immunotherapy for metastatic prostate cancer, although it is still early days. We believe the further study of nivolumab and ipilimumab in biomarker-selected patients with metastatic castration-resistant prostate cancer is warranted,” said Dr Mark Linch, Associate Professor (UCL Cancer Institute), Consultant Medical Oncologist (UCLH) and chief investigator of the trial

Encouragingly, the study has identified features associated with a positive response to the combination therapy, such as the presence of mutated BRCA1 or BRCA2 genes or high inflammatory infiltrate within the tumour. This

may provide a way to identify patients most likely to respond to the therapy. However, not all patients managed to complete the treatment, sometimes due to side effects from the treatment. The NEPTUNES trial is continuing to recruit men with mCRPC but using a better tolerated dose schedule which will hopefully provide even more benefit to patients.

This study is run by the CRUK-UCL Clinical Trials Centre and sponsored by UCL.

21 May 2021

Source: <https://www.ucl.ac.uk/cancer/news/2021/may/combination-immunotherapy-metastatic-prostate-cancer-shows-promise>

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Keenan: A Nose for Prostate Cancer; The Dog Will See You Now

Dogs are being trained to sniff out a variety of maladies from prostate cancer to COVID to malaria, as Freya the springer spaniel has been trained to detect. Courtesy, Medical Detection

Medieval doctors would slosh a patient's urine in a flask, rating it on colour charts — “yellow as of reduced lemon” or perhaps “bluish-grey, like camel skin.” Diagnosis could also be made by smelling, and even tasting, a nice fresh pee sample.

Today there are machines and even apps to spare humans from doing this. That said, we still have a lot to learn from nature.

That's why, in a lab in the U. K., a four-year-old wire-haired Vizsla named Midas and a seven-year-old labrador called Florin are being trained to sniff for the most aggressive form of prostate cancer. They work for Medical Detection Dogs, a charity that trains Medical Alert and Bio Detection dogs. Those are the same smart canines you see wearing a “Please Don't Pet Me – I'm Working” doggie vest.

Clare Guest is both the founder of Medical Detection Dogs and the lead author of a paper published recently in PLOS ONE, with co-authors from Harvard, MIT, and other prestigious U. S. universities.

“We've known for over 10 years now that dogs can detect cancer and can be trained to detect the odour of prostate cancer,” says Guest. Admitting that it isn't practical to have a specially trained dog on call in every hospital, “what we've been working towards is a way of understanding how dogs can do this fantastic thing, and how this might

be translated, perhaps, into an electronic device in the future.”

The paper reports substantial progress towards this goal. “The canine olfaction system was 71% sensitive and between 70 to 76% specific at detecting Gleason 9 prostate cancer,” wrote Guest and her colleagues. Sensitivity refers to how well the test catches people with the condition. Selectivity means that the test doesn't get confused by other conditions.



Dogs are being trained to sniff out a variety of maladies from prostate cancer to COVID to malaria, as Freya the springer spaniel has been trained to detect. Courtesy, Medical Detection Dogs PST

Selectivity can be an issue with the well-known prostate-specific antigen (PSA) test. There are lots of reasons for your PSA level to change. Some are very serious. Others, like an enlarged but otherwise benign prostate may be nothing to worry about. All are worth discussing with your doctor, at least to put your mind at rest.

Some of the treatments and even tests related to prostate cancer can have lasting negative effects. In a presentation at the annual meeting of the American Chemical Society, Amanda Siegel of Purdue University estimated that “about 60 per cent of men who get a biopsy to test for

prostate cancer don't need to get one.” It would be wonderful to have a way to give the test only to guys who need it.

One of the most promising ideas advanced by Guest is to combine information from doggie noses with artificial intelligence. The dogs are almost certainly reacting to specific volatile organic compounds (VOCs) in the urine sample. You've probably heard of VOCs in the paint store,

where it's a good thing to have low levels. Even if humans can't smell them, we can analyze VOCs through gas chromatography-mass spectroscopy (GC-MS).

The researchers fed the diagnostic information gained from the dogs into an artificial neural network, which can automatically learn to recognize patterns. This paid off in narrowing down where to look when searching for cancer biomarkers. A typical urine sample might have upwards of 1,000 VOCs, so the dog data narrowed the search for the sought-after biomarkers. It's

important to point out that these techniques were only tested on a small number of patients, using just two dogs.

Perhaps the biggest insight from this work is a sense of wonder at the nose of a dog. With 300 million sensors, compared to six million in humans, it should do a great job. But it also does a complex job – sorting out features that humans find baffling, even when displayed on a gas chromatograph printout.

As Guest explains, “The very nature of the GC-MS technique can be seen
(Continued on page 5)

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as being loosely analogous to biological olfaction: GC-MS peaks are not always correspondent to just one molecular species and fragments from different molecules but of equal charge/mass ratios might add to the same peak while fragments of the same molecule might appear as parts of various peaks."

Florin, that smart sniffer dog, has been flown to the Massachusetts Institute of

Technology to have her trained sense of smell analyzed and perhaps automated. Most experts feel that if scientists can create a robotic nose for prostate cancer, the concept will apply to many cancers, and other diseases as well.

With the advent of at-home COVID-19 testing, it's logical to ask if prostate cancer testing could soon be done by the patient. Home PSA tests are coming on to the market, though the

best advice in Canada is to speak with your doctor. Not only will that be easier financially, but all your records will also be in one official place. Even the details of your straw-coloured urine.

May 08, 2021 Dr. Tom Keenan

<https://calgaryherald.com/health/men/keenan-a-nose-for-prostate-cancer-the-dog-will-see-you-now>

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How Does Environmental Quality Affect Prostate Cancer Aggressiveness?

A study from researchers at the University of Illinois Chicago investigates the link between environmental quality and prostate cancer, finding that lower environmental quality is associated with an advanced-stage diagnosis of prostate cancer. The findings have been published in the journal *Prostate Cancer and Prostatic Disease*.

Given that prostate cancer is up to 57% heritable, the research team was interested in understanding how much environmental factors make up

the rest of that risk level. To do so, they looked at data from the environmental quality index (EQI) and the Surveillance, Epidemiology, and End Results Program (SEER). EQI data comes from environmental monitoring sources like the EPA to combine subdomain information on air, water, land, built, and sociodemographic.

"When we drilled down further into the subdomains of the EQI, we found that

some of the associations were stronger than others. Specifically, the land, water, and sociodemographic domains seem to be driving the association more than air or built domains," noted study co-author Dr. Michael Abern, who is an associate professor and director of urologic oncology at the University of Illinois College of Medicine.



Their analysis showed that residents living in areas with low-quality land, water and sociodemographic variables demonstrated the strongest association with prostate cancer being diagnosed at a later stage. Later diagnosis translates into real consequences for treatment outcomes, but early diagnosis has a nearly 100% five-year survival rate. Their study also considers sociodemographic factors such as health equity, showing that Black men

have a higher risk of metastatic prostate cancer at diagnosis than any other group.

The researchers say that their findings will help patients frame their diagnoses in their self-narratives. "When I see a patient with prostate cancer, they assume maybe they got it because of something they did. It is probably not. Not a lot is known about personal lifestyle choices that lead to prostate cancer. Diet, exercise and smoking have never had a very strong association with prostate cancer," Dr. Abern said. "Seeing a doctor and getting

screened is still the most important thing about getting diagnosed."

MAY 19, 2021

Kathryn DeMuth Sullivan

Sources: *Prostate Cancer and Prostatic Disease*, Eureka Alert

<https://www.labroots.com/trending/cancer/20496/environmental-quality-affect-prostate-cancer-aggressiveness>

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FDA Approves New Imaging Agent to Find Advanced Prostate Cancer

The approach won't replace traditional blood screening tests, but it could help guide doctors when cancer spreads.

The Food and Drug Administration has approved a new imaging agent to detect prostate cancer after it has spread to other parts of the body.

Experts say the tracer, made by medical imaging company Lantheus, will give doctors an important visual aid to guide them to metastatic prostate cancer cells that, before now, were difficult to spot.

Prostate cancer is the second leading cause of cancer deaths in men in the United States, after lung cancer, according to the American Cancer Society. More than 34,000 men die of the disease every year.

When prostate cancer spreads, it often goes into the bones, said Dr. Michael Morris, a medical oncologist at Memorial Sloan Kettering Cancer Center in New York City. That makes it difficult to detect using traditional imaging techniques.

"It's really hard to take pictures of what's going on inside of bone," Morris said, adding that traditional scans tend to find problems in the tissue surrounding bones, after damage has already been done.

"Now we don't have to wait for that," Morris said, who was involved with clinical trials of the tracer. "We can detect it much more clearly and much earlier than we could before."

The new technique uses a tracer molecule that seeks out a protein found on most prostate cancer cells called prostate-specific membrane antigen, or PSMA. The tracer, which is injected

into the bloodstream, lights up those cells during a PET scan.

A similar tracing agent, which also seeks out PSMA, was approved by the FDA in December for use at two California hospitals: the University of California, Los Angeles and the University of California, San Francisco. The facilities had been researching this kind of technology since 2015.



"We've been using it for many years and it works great," said Dr. Thomas Hope, director of molecular therapy in UCSF's Department of Radiology and Biomedical Imaging. "We can actually see where the disease is and now people are getting targeted radiation."

"It's redefining how we think about prostate cancer," he said.

The new approval will be the first such tracer for advanced prostate cancer commercially available nationwide.

The scan isn't meant to replace PSA testing, a common prostate cancer screening tool. PSA stands for prostate-specific antigen, a protein found in the blood. Instead, it's meant for men who have already been diagnosed with the disease.

The scan would be most useful for prostate cancer patients who have rising PSA levels after they have undergone treatment, including surgery and radiation, said Dr. Xiao Wei, an oncologist at Dana-Farber Cancer Institute in Boston. A rising PSA level would indicate that the cancer has spread elsewhere in the body.

While Wei and other prostate cancer experts agreed that the imaging would give them more information about

metastatic cancer, it remains unclear what they should do with the information.

"The huge looming question is, does it actually impact what we do for the patient? Will that help us improve outcomes?" said Dr. Justin Gregg, an assistant professor of urology and health disparities research at MD Anderson Cancer Center in Houston.

Prostate cancer treatment is often personalized, depending on a man's age, any other risk factors he might have or how aggressive the cells look under a microscope. Treatment, which can include radiation and removal of the prostate, can have significant side effects, including impotence and incontinence.

And not all metastatic prostate cancers will threaten a man's life.

"We may find deposits, but in an elderly man 75 or 85 years old, they might sit there and not require urgent treatment," said Dr. Derek Raghavan, president of the Levine Cancer Institute in Charlotte, North Carolina. "There is also a variant of prostate cancer that can be metastatic and actually not harm the patient for several years."

The new imaging is unable to determine which kinds of prostate cancer cells are likely to be more dangerous, Raghavan said.

"My guess is that as they develop the technology," he said, "they will develop a refined method for identifying those with a rapid growth potential."

By Erika Edwards, John Torres, M.D. and Lauren Dunn May 27, 2021

<https://www.nbcnews.com/health/health-news/fda-approves-new-imaging-tool-find-advanced-prostate-cancer-drugmaker-n1268621>

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Cleveland Clinic Researchers Identify New Drug Target For Treating Aggressive Prostate Cancer

According to new findings published in *Science Translational Medicine*, Cleveland Clinic researchers have identified a promising drug target for treating and preventing aggressive, drug-resistant prostate cancer.

The team, led by Nima Sharifi, M.D., of Cleveland Clinic's Lerner Research Institute, demonstrated that inhibiting the protein H6PD led to significantly reduced tumor sizes and improved survival among mouse models with drug-resistant prostate cancer. The H6PD levels also were elevated in biopsied patient tumors, suggesting the protein might be targeted in patients for treatment.

"New treatment approaches for drug-resistant prostate cancer are desperately needed," said Dr. Sharifi, director of Cleveland Clinic's Genitourinary Malignancies Research Center. "These findings suggest an entirely new strategy for treatment of men with this aggressive form of prostate cancer."

Enzalutamide, a current standard-of-care hormone therapy for metastatic prostate cancer, works by blocking androgen receptors, which are proteins that help drive cancer cells. While initially effective, most patients eventually develop resistance to the treatment. This resistance occurs when androgen receptors are blocked and cancer cells adapt to get their "fuel" from a similar receptor, called the glucocorticoid receptor.

These glucocorticoid receptors bind to and interact with the stress hormone cortisol. In an earlier study published in *eLife*, Dr. Sharifi and his team linked

enzalutamide resistance to increased tumor cortisol levels. They found that tumors typically express a protein called 11 β -HSD2, which inactivates cortisol. However, when this protein expression is inhibited in some tumors, cortisol and the glucocorticoid receptor are stimulated and become available for use by cancer cells.

"Taken together, our study findings suggest that pharmacologically inhibiting the H6PD protein can reverse drug resistance in prostate cancer cells," said Dr. Sharifi. "By blocking this



protein, we are able to prevent cancer cells from utilizing their backup fuel supply—cortisol and its receptor. When we block this pathway, tumors begin to become responsive to standard treatments again."

In this new study, the researchers demonstrated that, in addition to decreased expression of 11 β -HSD2, resistant tumors also have increased H6PD levels.

"With lower levels of 11 β -HSD2, which normally functions to cut off the fuel supply to drug-resistant cancer cells, the cells are free to continue to grow and spread unchecked," said Dr. Sharifi. "By inhibiting the H6PD protein, however, we were able to

reinstate anti-cortisol effects. This finding is key to better understanding how disruptions in cortisol metabolism contribute to cancer cells' growth and spread."

Dr. Sharifi's clinical collaborator Eric Klein, M.D., chair of Cleveland Clinic's Urology & Kidney Institute and a co-author on the study, said, "We found elevated levels of H6PD in both animal models and patient tissues, particularly after treating tumors with enzalutamide. These findings hold promise for novel

precision medicine approaches in the management of men with aggressive prostate cancer."

The researchers targeted H6PD with rucaparib, a drug already approved by the U.S. Food and Drug Administration. Dr. Sharifi collaborated with scientists from Cleveland Clinic's Center for Therapeutics Discovery to identify what parts of

rucaparib are chemically necessary to inhibit the protein.

Researchers administered enzalutamide to mouse models of aggressive prostate cancer that expressed H6PD and those where the protein was blocked with rucaparib. The models where H6PD was blocked had significantly smaller tumors and longer progression-free survival following enzalutamide treatment.

by Cleveland Clinic MAY 26, 2021

Source: <https://medicalxpress.com/news/2021-05-cleveland-clinic-drug-aggressive-prostate.html>

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FUTURE MEETINGS 2021

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Watch this space
 for information
 on the latest status.

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