PCCN Markham

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PEER SUPPORT MEETING

Tuesday, February 11, 2020 - 7:30PM

St. Andrews Presbyterian Church – Main St Markham

Rose Room - Downstairs

(Free Parking & Room access off George Street)

Peer Support Session

Meetings provide an opportunity for you to talk in complete confidence with prostate cancer survivors.
There's usually someone at a meeting who has had the treatment you are considering and this gives you an opportunity to talk directly to men who've been through the various treatments.
Group provides an opportunity to talk with others about managing life with prostate cancer.
Note: ***we cannot give medical advice, but can share our knowledge of treatments and experiences.***

ALL WELCOME!!

IN THIS ISSUE …

Our March 10 Speaker will be Dr. Rus Sethna, Chief of Psychiatry - MSH
All Welcome

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Researchers Identify New Source of Drug Resistance in Prostate Cancer

Published: January 27, 2020

SUMMARY: Drug resistance in prostate cancer remains a significant challenge to successful treatment, but a new paper shines light on one cause of resistance to androgen receptor-targeting drugs.

For designers of targeted drugs, the biggest bullseye in prostate cancer has been the androgen receptor — a specialized net on prostate cells that snares androgen molecules to spur the cells' growth. Drugs that block, or inhibit, the receptor can halt the cancer, but not all patients benefit from them, and nearly all those who *do* respond eventually become resistant.

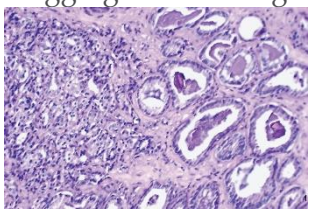
Scientists have found that resistance often occurs because the androgen receptor (AR) regains the ability to switch on the cell's growth machinery even when the receptor is plugged with a drug molecule. But researchers also know that cancer cells usually harbor more than one backup plan: They have a variety of ways of circumventing a drug that initially worked well.

In a recent paper, Dana-Farber investigators uncovered one such mechanism: surplus production of a protein called CREB5. They found that advanced prostate cancers with an overactive *CREB5* gene, or with too many copies of it, were able to proliferate after treatment with one of the newest AR inhibitors.

The discovery, published in *Cell Reports*, suggests that drugs targeting CREB5 could be effective in prostate cancers resistant to AR-blocking drugs. Although such drugs do not yet exist, they are under development.

"CREB5 has been shown to be overexpressed in some glioblastoma brain cancers and kidney cancers," said Dana-Farber's Justin Hwang, PhD, who led the study with William Hahn, MD, PhD, the Institute's chief scientific officer. "This suggests that targeting CREB5 could be useful in these malignancies as well as prostate cancer."

Flagging the *CREB5* gene



A section of a prostate gland containing numerous cancer cells.

Investigators first flagged the *CREB5* gene as a potential culprit in AR inhibitor resistance in research beginning in 2015. Hahn's team screened 17,255 genes and examined more than 1,000 prostate tumor samples to see which genes were abnormally active and promoted resistance to the AR inhibitor enzalutamide. The standout gene — the one whose activity jumped highest in these samples — was *CREB5*.

In the new study, researchers conducted an array of tests to determine whether *CREB5* does in fact drive an enzalutamide resistance pathway. In laboratory cell lines, animal models, and three-dimensional models of prostate tumors, the investigators found that overexpression of *CREB5* led to resistance of all AR inhibitors tested, including enzalutamide.

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"We found that over 25% of the clinical samples had very high levels of *CREB5* activity," Hwang said. The increase could be due to excess copies of the *CREB5* gene at either the DNA or RNA level.

Hahn's team found that when prostate cancer cells are treated with enzalutamide, CREB5 interacts with key genes to perk up the AR, increasing its output of cell growth signals.

CREB5 is a transcription factor — controlling how quickly genetic information is transferred from DNA to RNA — a class of proteins that is notoriously difficult to thwart with small molecule drugs. But, Hwang notes, it has a unique structure relative to other transcription factors and targeting this structure may interfere with its activity in cancer cells.

https://blog.dana-farber.org/insight/2020/01/researchers-identify-new-source-of-drug-resistance-in-prostate-cancer/

Healthy older men may benefit from prostate cancer screening

medwireNews: 01-2020 | By Shreeya Nanda

The risk for clinically significant prostate cancer rises with age, report researchers who believe that this should be taken into account in the optimization of screening practices.

The team drew on the Cancer Registry of Norway to identify 20,356 men who were diagnosed with prostate cancer in 2014–2017 and assigned them to prostate cancer risk stratification categories based on contemporary definitions. The specific categories were low, favorable intermediate, unfavorable intermediate, high, regional, and metastatic.

There was a significant association between age and prostate cancer risk groups, with older men more likely to have more advanced disease. For example, the incidence of at least high-risk disease was 29.3% among men aged 55–59 years, rising to 39.1%, 60.4%, and 90.6% among those aged 65–69, 75–79, and 85–89 years, respectively. The corresponding rates of low-risk prostate cancer were 24.0%, 17.9%, 10.2%, and 4.1%.

Older men also had a significantly greater likelihood of having clinically significant disease at diagnosis, regardless of whether it was defined as all cases of at least intermediate-risk or all cases of at least unfavorable intermediate-risk prostate cancer.

Additionally, age-specific incidence rates (ASIRs) based on Norwegian population data increased across all risk categories until the ages of 65–69 years, at which point the low- and intermediate-risk cases tailed or leveled off, but high-risk cases continued to rise up to the ages of 75–79 years, declining thereafter.

Of note, the ASIR for high-risk prostate cancer was 408.3 per 100,000 men in the 75–79 year age group, which was more than sixfold greater than the ASIR for high-risk disease in the 55–59 year group, at 61.6 per 100,000 men.

The Gleason score was available for 18,665 cases, and analysis of these patients showed a significant association between age and Gleason score, such that older age at diagnosis correlated with a higher Gleason score at diagnosis. For instance, the proportion of individuals with a Gleason score of 8–10 was 16.5% in the 55–59 year age group, 23.4% in the 65–69 year age group, 37.2% in the 75–79 year age group, and 59.9% in the 85–89 year age group.

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In light of these findings, Tyler Seibert (University of California San Diego, La Jolla, USA) and collaborators suggest in *Cancer* that some healthy men in older age groups "could plausibly benefit from screening because of their high risk of aggressive disease and otherwise good life expectancy."

They continue: "Decision-making guidelines generally emphasize shared decision making for men aged 50 to 69 years and do not encourage screening of men aged 70 to 75 years, but perhaps the latter should be reconsidered for otherwise healthy men."

The study authors add a word of caution, however, noting that "[a]lthough our data suggest that screening older men may identify more clinically significant [prostate cancer], it is acknowledged that our data do not prove that screening could influence important clinical outcomes such as survival and quality of life. In addition, the risks of low-risk disease overdiagnosis must be considered."

https://oncology.medicinematters.com/prostate-cancer/risk-factors/healthy-older-men-may-benefit-from-prostate-cancer-screening/17589770

New drug target for prostate cancer found in the non-coding genome

1/23/2020

Dr. Mathieu Lupien, Senior Scientist, Princess Margaret Cancer Centre, is one of the first researchers to realize that the non-coding DNA holds critical elements that not only control the activity of genes, but also play a major role in many diseases. (Photo: Images by Delmar)

Scientists at Princess Margaret Cancer Centre have identified the drivers of a crucial gene involved in prostate cancer, revealing new targets for drug design.

Researchers identified a set of cis-regulatory elements – namely enhancers and the promoter – in the non-coding region of the genome, which affect the expression of FOXA1 gene, one of the major drivers or oncogenes involved in prostate cancer development.

FOXA1 has long been recognized as playing an important role in malignancy, but it is one of the most challenging targets for drug development in cancer.

Often termed "undruggable," it is extremely difficult to inhibit due to its lack of easily accessible "pockets" for small molecule therapies to slip into to break the deadly uncontrolled cell growth leading to cancer.

Scientists the world over are looking at different ways to target FOXA1, since it is implicated in many cancers including breast, prostate, lung, thyroid and esophageal squamous cell carcinomas.

"To track a tumour, we also have to look at the non-coding space in its DNA because that's where gene expression – the switching on or off of a gene – happens," explains Dr. Mathieu Lupien, Senior Scientist at Princess Margaret Cancer Centre and the senior author of this latest research.

"We can't dismiss what's going on in the non-coding space because that is what fuels differences in expression in genes. To fully understand a tumour, we have to explore the whole genome – the genes and the non-coding space."

Scientists have begun mining the dark or non-coding portion of the genome – about 98 per cent of the genome – as a potential source of new targets for drug development.

Dr. Lupien, who is also an assistant professor with the University of Toronto's Department of Medical Biophysics, is one of the first researchers to realize that hidden amongst the non-coding DNA are crucial elements that not only control the activity of thousands of genes, but also play a major role in many diseases. Exploring this area could provide important sequencing clues for potential cures.

Dr. Lupien's current research, entitled "Noncoding mutations target cis-regulatory elements of the FOXA1 plexus in prostate cancer" is published in *Nature Communications*, Jan. 23.

Researchers at the Princess Margaret have identified a set of cis-regulatory elements in the non-coding ("dark") genome, which affect the expression of FOXA1 – a gene that is a known driver of prostate cancer development. Now, there may be opportunity to develop more precise therapies against prostate cancer. (Video: UHN)

The research team examined 200 human prostate tumours and identified six mutated cis-regulatory elements which control FOXA1 expression. They further demonstrated that removing these elements reduced FOXA1 expression and impaired growth of prostate cancer cells.

"Because of the difficulties in targeting FOXA1 with drugs, we had to find alternative targets to block its function," says Dr. Lupien. "We found these targets by identifying regulatory elements in the non-coding DNA required for FOXA1 expression."

This allows us to expand our tool kit of potential therapies against prostate cancer, adds Dr. Lupien, because this regulatory web represents a more precise target against cancer.

Prostate cancer is the second most commonly diagnosed malignancy among men worldwide, with an estimated 1.3 million new cases worldwide in 2018.

In Canada, it is estimated that in 2019:

- 22,900 men will be diagnosed with prostate cancer. This represents 20 per cent of all new cancer cases in men in 2019.
- 4,100 men will die from prostate cancer. This represents nine per cent of all cancer deaths in men in 2019. Treatments typically fail in 30 per cent of patients within 10 years, resulting in cancer spreading to other sites. Despite the efficacy of anti-androgen therapies for metastatic cancer, recurrence ultimately develops into a lethal cancer. This spurs our need to improve our biological understanding of how prostate cancer develops, and to find novel strategies to treat patients.

This research is supported by the Canadian Institutes of Health Research, Prostate Cancer Canada (Movember), Ontario Institute for Cancer Research, Princess Margaret Cancer Foundation, Canadian Cancer Society, Terry Fox Research Institute and the Dutch Cancer Society KWF/Alpe d'HuZes.

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New drug helps extend survival rate of men with advanced prostate cancer: B.C. Cancer Agency study

At two years, advanced prostate cancer patients taking the trial drug, in addition to their standard treatment, had a 52% lower risk of cancer spread or death.

Vancouver Sun Updated: January 7, 2020

Dr. Kim Ch, who led a clinical trial which found that over half of patients who used a new type of hormone-reducing medication saw a reduction in their risk of cancer progression and a 33% improvement in overall survival, in Vancouver BC., June 10, 2019. NICK PROCAYLO / PNG

By: Pamela Fayerman

A new drug has helped reduce the risk of death by 33 per cent in men with prostate cancer that has spread, according to the results of an international trial led by the B.C. Cancer Agency's Dr. Kim Chi.

The double-blind study on the androgen receptor inhibitor drug called apalutamide was conducted in 23 countries at 260 cancer centres. It involved 1,052 men whose median age was 68. The study was sponsored by Janssen, the drug company who makes apalutamide.

At two years, those taking the treatment drug in addition to their standard treatment had a 52 per cent lower risk of cancer spread or death.

The findings of the TITAN (Targeted Investigational Treatment Analysis of Novel Anti-androgen) trial which began in 2015 are published in the New England Journal of Medicine (NEJM).

Results were also recently presented by Chi at the annual meeting of the American Society of Clinical Oncology.

Chi, an oncologist, said overall survival rate is only about five years once prostate cancer has spread beyond the prostate so new treatments are desperately needed. The percentage of patients who took the drug whose cancer did not spread was 68.2 per cent, but in the placebo group the proportion was 47.5 per cent. There was a 33 per cent reduction in the risk of death for those who took the drug.

After about two years, 82 per cent of men in the investigational drug group were alive compared to 74 per cent on placebo. Men in both groups also took standard male hormone deprivation therapy showing that combination therapy helps to improve survival. Male hormones (androgens) like testosterone feed prostate tumours and currently, men with metastatic cancer are put on hormone deprivation treatment that has been

the standard of care for many decades. Apalutamide, also called Erleada, is said to more completely block male hormones.

Chi said the drug is "not toxic" and there were no significant differences

in the proportion of study participants in the intervention or placebo groups who experienced side effects, but skin rashes were just over three times more common in the drug group.

The drug has already been approved in Canada for certain patients with hormone-resistant, non-metastatic cancer but Chi said now that it is showing benefit for patients whose cancer has spread, he expects the drug will be approved by Health Canada for those patients as well, perhaps later this year. After that approval, provinces will have to decide on whether to expand funding for the drug, which costs about $3,000 a month. Chi said he expects more Canadian patients will have access to it next year.

"This is a next generation, better-designed androgen inhibitor and we really need better drugs for those with metastatic prostate cancer," Chi said.

"There's a critical need to improve outcomes for these patients and this study suggests this treatment can prolong survival and delay the spread of the disease."

Chi was also a co-author on another drug trial, the results of which were published in the same issue of the NEJM medical journal. The ENZAMET trial, as it was called, is on a drug called enzalutamide (Xtandi). The results of that trial were similarly favourable.

About 2,700 men will be newly diagnosed with prostate cancer in B.C. this year. More than 600 men will die from it.

pfayerman@postmedia.com Twitter: @MedicineMatters

"You Have Prostate Cancer"!

A prostate cancer diagnosis can change your life. You may be in shock and you will most certainly go through a range of different emotions, most of which are related to anxiety and depression. You may feel sad, numb, angry, indifferent, anxious and many other emotions. These feelings may change frequently and with different levels of intensity. If you are single, you may find yourself feeling very isolated and having to reach out more to friends and professionals for comfort and support. If you are in a relationship, you may find yourself feeling guilty for thinking you are being a burden to your partner and worrying about the impact on them emotionally and financially.

Grieving is a complex process and doesn't follow logic or specific timeframes. Being diagnosed with prostate cancer may make you feel as though you have lost control of your body – and your life. You may be grieving unfinished business and unfulfilled expectations. As difficult as it can be, try to think about what positive actions you can take now to make you feel more at peace with your situation. Be patient and gentle with yourself and don't be afraid to reach out to others who might want to support you, but don't know how. Tell them how they can help, even if it just means spending quiet time with you. Sometimes a respectful silence can be healing and "enough" for some people.

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Keep in mind that your support network can include friends, support groups, church and spiritual groups and your healthcare team (e.g., family doctor, oncologist, social worker, psychologist, sex therapist).

Tips to Help

Here are a few ways to maintain mental and emotional wellness during your cancer journey:

- Be honest and clear with the people who you identify as wanting support from
- Share only the information you're comfortable sharing. If you're not comfortable sharing something about your diagnosis or treatment then don't
- Make a list of how each person can help you during this time (for example, drive you to appointments, help with chores, listening when you need someone to talk to)
- Ask your support network for the assistance you need, remembering that your needs may change as you move through your cancer experience
- Use relaxation techniques frequently such as deep breathing and meditation
- Take a break from everyday routine and make time for things you enjoy
- Get physical activity regularly. It has been shown to reduce anxiety and depression
- Join a support group. It sometimes helps talking to others who have gone through or are currently dealing with a similar experience
- Reach out to your healthcare team if you are finding it hard to cope with how you are feeling.
  https://www.prostatecancer.ca/Prostate-Cancer/Treatment/Side-Effects-of-Treatment/Mental-and-Emotional-Side-Effects

Is it true that pomegranate juice may slow the growth of prostate cancer?

Answer From Erik P. Castle, M.D.

Some early research suggested that drinking pomegranate juice slowed the progression of prostate cancer, but additional research failed to confirm those results.

For example, in some studies of men with recurrent prostate cancer and rising prostate-specific antigen (PSA) levels, researchers found that drinking pomegranate juice or taking pomegranate juice extract significantly slowed the rate at which PSA was rising (PSA doubling time). A longer PSA doubling time can indicate that the cancer may be progressing less rapidly.

But these studies didn't use a control group or a placebo group. Later studies using a placebo-controlled design found no benefit for pomegranate juice extract.

If you choose to drink pomegranate juice, talk with your doctor first. Although pomegranate juice is generally safe, there is evidence that it may affect how your body processes certain prescription medications. Those medications include the blood thinner warfarin (Coumadin, Jantoven) and some drugs used to treat high blood pressure and high cholesterol.

https://www.mayoclinic.org/diseases-conditions/prostate-cancer/expert-answers/pomegranate-juice/faq-20058204

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Eating More Vegetables Did Not Affect Prostate Cancer Progression

Men with early stage prostate cancer did not show benefits from a vegetable-rich diet.

By Nicholas Bakalar Jan. 20, 2020

Men with early stage prostate cancer are often advised to increase their intake of vegetables to lower the risk for progression to more serious disease. But now a randomized trial has found that vegetables, whatever other health benefits they may confer, have no discernible effect on prostate cancer progression.

In a two-year study published in JAMA, researchers randomly divided 478 patients with biopsy-confirmed early stage prostate cancer into two groups. Men in the first group were enrolled in a behavioral counseling program, with each assigned a counselor who, with repeated telephone calls, encouraged them to eat at least seven daily servings of fruits and vegetables. The second were simply given written information about diet and prostate cancer.

Diet interviews and blood tests for carotenoid concentrations showed that compared with the controls, the intervention group consumed significantly more vegetables. They also ate less red meat and less fat.

But there was no difference between the groups in time to progression to higher grade tumors as measured by increases in prostate specific antigen levels or by repeated biopsy.

The lead author, Dr. J. Kellogg Parsons, a professor of urology at the University of California, San Diego, said that improved diet has been shown to be helpful in previous epidemiological studies, but "unfortunately that isn't the case, probably because cancer is a very complex disease, and the answer is not as simple as eating more vegetables."

"The study doesn't give license for folks to not eat a healthy diet," he added. "Lots of other research in prostate and other cancers has shown that men who are more robust and healthier in general tolerate their treatment much better."

www.nytimes.com

QUOTABLE

"Everyone you meet is fighting a battle you know nothing about. Be kind. Always." **Brad Meltzer**

"There is little difference in people, but that little difference makes a big difference. The little difference is attitude. The big difference is whether it is positive or negative." -- W. Clement Stone

"A happy house is one in which each spouse grants the possibility that the other may be right, though neither believes it."-- Don Fraser

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Prostate Cancer Support Group

Meets the 2nd Tuesday
Every month
September – June
St. Andrew's Presbyterian Church
143 Main St Markham

The Markham PCCN Prostate Support Group is generously supported by Dr. John DiCostanzo, Astellas Pharma, St. Andrews Presbyterian Church, PCCN, and the Canadian Cancer Society.

The group is open to all; survivors, wives, partners, relatives and those in our community who are interested in knowing about prostate health. Drop by St Andrews Presbyterian Church 143 Main Street Markham at 7:30PM, the 2nd Tuesday every month from September to June. The information and opinions expressed in this publication are not endorsements or recommendations for any medical treatment, product, service or course of action by PCCN Markham its officers, advisors or editors of this newsletter.

Treatment should not be done in the place of standard, accepted treatment without the knowledge of the treating physician.

The majority of information in this newsletter was taken from various web sites with minimum editing. We have recognized the web sites and authors where possible.

PCCN Markham does not recommend treatment, modalities, medications or physicians. All information is, however, freely shared.

Email *markhampccn@gmail.com*

We look forward to your feedback and thoughts. Please email suggestions to markhampccn@gmail.com

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