East Lancashire Prostate Cancer Support Group Newsletter

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What's Inside

By boosting innate immunity, researchers eradicate aggressive prostate cancer in mice Drug activates neutrophils instead of T cells, leading to cancer clearance

Date: March 8, 2017

Source: University of Chicago Medical Center

Summary:

Cabozantinib, an FDA-approved drug for patients with certain types of thyroid or kidney cancer, was able to eradicate invasive prostate cancers in mice by causing tumor cells to secrete factors that entice neutrophils -- the first-responders of the immune system -- to infiltrate the tumor. This novel approach, utilizing the innate immune system, produced near-complete clearance of invasive prostate cancers within 48 to 72 hours.

Cabozantinib, a drug already used to treat patients with certain types of thyroid or kidney cancer, was able to eradicate invasive prostate cancers in mice by causing tumor cells to secrete factors that entice neutrophils -- the first-responders of the immune system -- to infiltrate the tumor, where they triggered an immune response that led to tumor clearance.

The drug, marketed as Cometriq®, enhances the release of specific chemical signals, known as CXCL12 and HMGB1, from pros-

tate cancer cells. These signals cause the neutrophils, produced in the bone marrow, to flock to the tumor and attack the cancerous cells. In mice with aggressive prostate cancer, it produced near-complete clearance of invasive prostate cancers within 48 to 72 hours.

The authors of this study (published online March 8, 2017, in Cancer Discovery) note that this is the first demonstration that a drug of this type (a tyrosine kinase inhibitor) could activate innate anti-tumor immunity, resulting in the eradication of invasive cancer. They also suggest it could be used as part of a novel approach to combination cancer immunotherapy.

"We saw dramatic anti-tumor responses," said the study's lead author and investigator, medical oncologist and physician-scientist Akash Patnaik, MD, PhD, Assistant Professor of Medicine, Director of the Developmental Therapeutics Laboratory and Attending Physician within the Genitourinary Oncology Program at the University of Chicago Medicine. "We used a difficult-to-treat, aggressive prostate cancer mouse model. We were very surprised to see complete eradication of the most invasive, poorly differentiated tumors within days."

"The results of this study were really unexpected," said co-author Lewis Cantley, PhD, Director of the Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine in New York City.

Cabozantinib, FDA approved in 2012 for metastatic medullary thyroid cancer and in 2015 for advanced renal cell carcinoma, was recently tested in the COMET-1 trial in men with metastatic prostate cancer. But the results were disappointing. Some of the patients had a good response, but many did not.

"Why some of these patients responded and others did not was unclear," Cantley said.

Following the dramatic results in a subset of advanced prostate cancer patients in the Phase II trial, Patnaik and colleagues began testing the drug in the lab. In their mouse model for prostate cancer, cabozantinib caused dramatic shrinkage of the tumors within a few days. But when tested on prostate cancer cell lines in a petri dish, it had relatively little effect.

Why was there a dramatic in vivo effect with little ex vivo effect? Patnaik and colleagues wondered.

"The drug was not actually killing the tumor cells," Cantley said. "Instead, it was inducing them to release factors that stimulated an attack by the innate immune system."

The key was the neutrophil-attracting chemical signals CXCL12 and HMGB1, released by tumor cells. When the researchers blocked production of these signals, the drug was no longer effective. The neutrophils -- Patnaik refers to them as the "suicide bombers of the immune system" -- never engaged in battle.

"Our findings could also explain why some patients in the COMET-1 trial did not benefit from the drug," Patnaik said. "This Phase-III trial included patients who had already received aggressive chemotherapy, which may have compromised their immune systems."

While additional research is being done to understand how cabozantinib accomplishes this effect, "this paper raises the possibility that a new class of drugs could be developed to treat cancers by stimulating attack by neutrophils," Cantley said.

For several years now, the most exciting development in cancer research has been the emergence of immunotherapies, especially checkpoint blockade drugs such as ipilimumab, nivolumab and pembrolizumab that enable the adaptive immune system, in this case T cells, to enter and attack tumors. But there has been little attention paid to inducing the innate immune system, such as neutrophils, to go after tumors.

"Neutrophils can be just as potent as T cells," Patnaik stated. He now hopes to use them in

combination.

"Based on our results showing that cabozantinib can activate innate immunity and overcome an immunosuppressive tumor microenvironment, we are planning clinical trials to test the combination of cabozantinib and T cell checkpoint immunotherapy in specific subtypes of advanced kidney and prostate cancer. Our goal," Patnaik said, "is to enhance long-term anti-cancer responses from activating both innate and adaptive immunotherapy."

Story Source:

Materials provided by University of Chicago Medical Center. Note: Content may be edited for style and length.

Journal Reference:

Akash Patnaik, Kenneth D. Swanson, Eva Csizmadia, Aniruddh Solanki, Natalie Landon-Brace, Marina P. Gehring, Katja Helenius, Brian M. Olson, Athalia R. Pyzer, Lily C. Wang, Olivier Elemento, Jesse Novak, Thomas B. Thornley, John M. Asara, Laleh Montaser, Joshua J. Timmons, Todd M. Morgan, Yugang Wang, Elena Levantini, John G. Clohessy, Kathleen Kelly, Pier Paolo Pandolfi, Jacalyn M. Rosenblatt, David E. Avigan, Huihui Ye, Jeffrey M. Karp, Sabina Signoretti, Steven P. Balk, Lewis C. Cantley. Cabozantinib Eradicates Advanced Murine Prostate Cancer by Activating Anti-Tumor Innate Immunity. Cancer Discovery, 2017; CD-16-0778 DOI: 10.1158/2159-8290.CD-16-0778

Starving prostate cancer with what you eat: Apple peels, red grapes, turmeric

Date: June 6, 2017

Source: University of Texas at Austin

Summary:

When you dine on curry and baked apples, enjoy the fact that you are eating something that could play a role starving -- or even preventing -- cancer. New research identifies several natural compounds found in food, including turmeric, apple peels and red grapes, as key ingredients that could thwart the growth of prostate cancer.

When you dine on curry and baked apples, enjoy the fact that you are eating something that could play a role starving -- or even preventing -- cancer.

New research from The University of Texas at Austin identifies several natural compounds found in food, including turmeric, apple peels and red grapes, as key ingredients that could thwart the growth of prostate cancer, the most common cancer afflicting U.S. men.

Published online this week in Precision Oncology, the new paper uses a novel analytical approach to screen numerous plant-based chemicals instead of testing a single agent as many studies do, discovering specific combinations that shrink prostate cancer tumors.

"After screening a natural compound library, we developed an unbiased look at combinations of nutrients that have a better effect on prostate cancer than existing drugs," says corre-

sponding author Stefano Tiziani, assistant professor in the Department of Nutritional Sciences and Dell Pediatric Research Institute at UT Austin. "The beauty of this study is that we were able to inhibit tumor growth in mice without toxicity."

During the past decade, some cancer research has highlighted the potential therapies found in plants, including chemicals found in foods such as turmeric, apple peels and green tea. These compounds minimize one of the risk factors for cancer, inflammation within the body. People who have chronic inflammation because of chronic infection, autoimmune disease or conditions such as obesity have a higher cancer risk because of damage to normal cells.

The researchers first tested 142 natural compounds on mouse and human cell lines to see which inhibited prostate cancer cell growth when administered alone or in combination with another nutrient. The most promising active ingredients were then tested on model animals: ursolic acid, a waxy natural chemical found in apple peels and rosemary; curcumin, the bright yellow plant compound in turmeric; and resveratrol, a natural compound common to red grapes or berries.

"These nutrients have potential anti-cancer properties and are readily available," says Tiziani. "We only need to increase concentration beyond levels found in a healthy diet for an effect on prostate cancer cells."

The new research paper also demonstrates how the plant-based chemicals work together. Combining ursolic acid with either curcumin or resveratrol prevents cancer cells from gobbling something that they need to grow, glutamine. This is a neat solution: blocking the uptake of a nutrient needed by prostate cancer cells with nutrients that are commonly in the human diet.

Story Source:

Materials provided by University of Texas at Austin. Note: Content may be edited for style and length.

Journal Reference:

Alessia Lodi, Achinto Saha, Xiyuan Lu, Bo Wang, Enrique Sentandreu, Meghan Collins, Mikhail G. Kolonin, John DiGiovanni, Stefano Tiziani. Combinatorial treatment with natural compounds in prostate cancer inhibits prostate tumor growth and leads to key modulations of cancer cell metabolism. npj Precision Oncology, 2017; 1 (1) DOI: 10.1038/s41698-017-0024-z

A Social Event with the Walnut Group

We have hired a 36 seater coach for a trip to York. The ladies can look at the city while some of the gents want to look at the trains.

I am sure we will have some spare seats and I wonder if any of you group would be interested.

We need to complete the York trip arrangements.

The details are below and I am sure we could arrange an M65 pickup for EastLancs if needed.

The cost will be a maximum of £18 and we leave Vine house at 8.00am and return from York at 6.00pm on Friday the 30th June.

These details were agreed at the last meeting, allowing time for an early tea before leaving.

Contact riley.d7@sky.com

From Left to Right Hazel Goulding (Treasurer) Leon D Wright (IT Admin) Stuart Marshall (Secretary) Steve Laird (Vice Chairman) Dave Riley (Chairman)

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We are a group of local people who know about prostate cancer. We are a friendly organisation dedicated to offering support to men who have had or who are experiencing the effects of this potentially life threatening disease.

The East Lanc's Prostate Cancer Support Group offers a place for free exchange of information and help for local men and their supporters (family and friends) who may be affected by this increasingly common form of male cancer.

At each meeting we strive to be a happy, supportive and upbeat group of people; encouraging open discussion on what can be a very difficult and perhaps for some an embarrassing subject. We have lively, informative, interactive, sharing and above all supportive meetings.

"Having a Laugh" Impotence & Viagra

A lady goes to the doctor and complains that her husband is losing interest in sex. The doctor gives her a pill, but warns her it is still experimental and tells her to slip it into his mashed potatoes at dinner. So, that night at dinner, she does. About a week later she's back at the doctor's office. She says, "Doc, the pill worked great! I put it in the potatoes like you suggested. It wasn't five minutes and he jumps up, rakes all the food and dishes off the table, grabs me, rips all my clothes off and ravishes me right then and there on the table." The doctor says, "I'm sorry, we didn't realize the pill was that strong. The foundation will be glad to pay for any damages." "Naah..." she says, "that's okay. We wouldn't go back to that restaurant anyway."

Jeff Stelling ’s March for Men

He's made it!

On Friday 16 June, Jeff Stelling finished his epic 400-mile journey from Exeter to Newcastle. He marched for better diagnosis, better treatment and better support. He marched to raise awareness of a disease that kills one man every hour. He marched for men, and you can help Jeff make a difference by sponsoring him.

This weekend, we're asking you to put your boots on for prostate cancer and join hundreds of us for a sponsored walk in Leeds, London or Glasgow. No need to sign up in advance - just come along at 10am, and bring £10 for your registration fee.

London - Saturday 17 June, Olympic Park Stratford. 2k, 5k or 10kk route.

Leeds - Sunday 18 June, Roundhay Park. 2k, 8k or 16k route.

Glasgow - Sunday 18 June, Pollok Country Park. 2.5k, 8k or 16k route.

Classic Vehicle Show

Formerly the Towneley Classic Car Show, the Burnley Classic Vehicle Show is hosted by The Rotary Club of Burnley in conjunction with Burnley Borough Council, it is now in it's 33rd year and is more popular then ever.

Held in the grounds of Towneley Hall it is a family friendly event with lots to see and do for everyone. There is a small funfair for the children, access to Towneley Hall and the grounds (which include walks, nature trails and even a pitch and putt course), plenty of stalls with information about local charities and attractions, plenty of lovely food with a bar and of course we can't forget the classic vehicles themselves!

Best of all, the entire event is free (although there is opportunity to donate) and all money raised is distributed by the Rotary Club of Burnley to selected charities.

This years show looks set to be bigger and better than ever, with local radio station 2BR keeping us entertained!

The next event is on Sunday 25th of June 2017 and we look forward to seeing you.