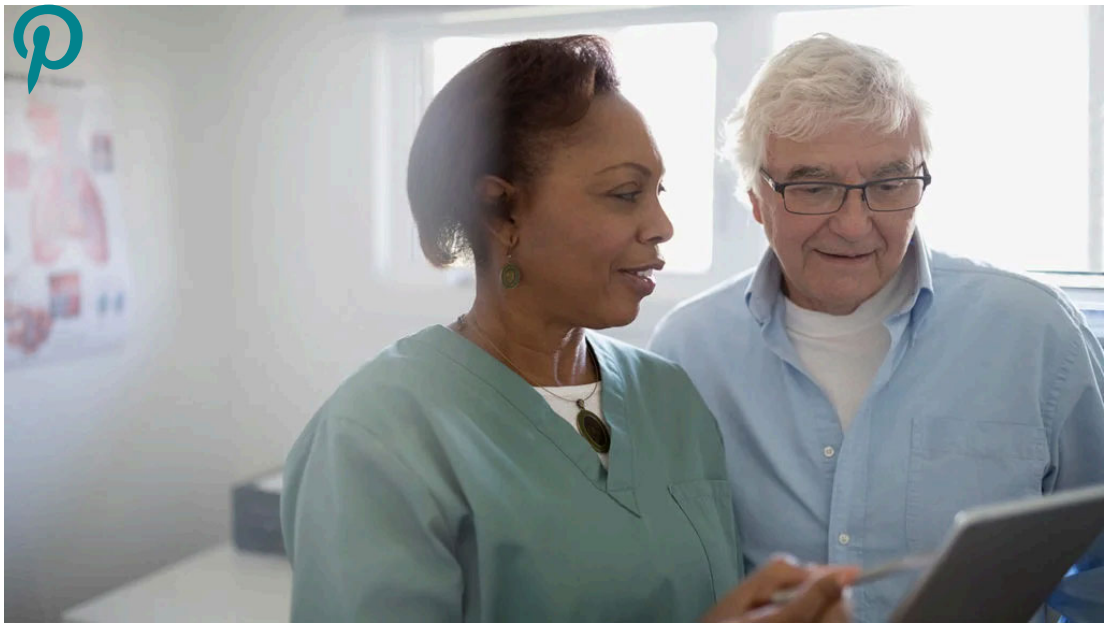
HEALTH NEWS

How Prostate Cancer Becomes Resistant to Treatment

Written by George Citroner on February 28, 2019

MORE IN PROSTATE CANCER PROSTATE CANCER

treatments.



Researchers say a molecular “switch” can lead to prostate cancers becoming treatment-resistant. Getty Images

It’s the second most diagnosed cancer in men, just behind skin cancer.

It’s typically slow growing and there are life-saving treatments available.

But, sometimes the cure can make prostate cancer more deadly.

A new study released today from Sanford Burnham Prebys Medical Discovery Institute in La Jolla, California, details how prostate cancer can be transformed into an aggressive and incurable disease — by the treatment that's supposed to save lives.

Hormones called androgens stimulate prostate cancer cells to grow. Newly developed anti-androgen therapies for prostate cancer are a major advance in the fight against this disease.

Testosterone and dihydrotestosterone (DHT) are the main androgens in men. Lowering androgen levels or stopping them from getting into prostate cancer cells can make those cells shrink or grow more slowly.

However, men who receive these new treatments are also more likely to develop a deadly, treatment-resistant cancer called neuroendocrine prostate cancer (NEPC). There are no effective treatments for this type of cancer.

In their study, researchers analyzed tissue samples from men with NEPC as well as prostate cancer cell lines and a mouse model of NEPC created by the researchers.

They said they discovered a molecular "switch" that triggers this cancer to become treatment-resistant after anti-androgen treatment.

Creating resistant cancers

NEPC previously accounted for only 2 to 5 percent of all diagnosed prostate cancer cases, according to Dr. Maria Diaz-Meco, a professor in the Cancer Metabolism and Signaling Networks Program at Sanford Burnham Prebys Medical Discovery Institute and lead author of the study.

That's no longer the case. It's now approaching 30 percent.

"Things have changed a lot due to the new generation of androgen inhibitors, which are much more potent than earlier ones," Diaz-Meco noted.

The androgen treatments have increased survival against tough-to-treat prostate cancer as well as those where tumors have spread.

"But these treatments can also cause cancers to become resistant, like bacteria develop antibiotic resistance," Diaz-Meco said. "The incidence of these neuroendocrine tumors after targeted treatment is now much higher."

NEPC is undetectable by PSA test

The PSA test is a blood test used to screen for prostate cancer. PSA is a protein produced by both cancerous and noncancerous tissue in the prostate.

The test can detect high levels of PSA that may indicate prostate cancer, but the treatment-resistant cancers can sometimes avoid detection.

"The problem with these new, resistant cancer cells is that they're androgen indifferent, or androgen independent, which is why the treatments stop working and why they don't increase PSA levels," said Diaz-Meco.

Undetected, the cancer will eventually move to other places, usually the liver, lungs, and bone.

Surprising discovery

While there is no cure for NEPC, Diaz-Meco's research may eventually lead to new treatment options.

She emphasized that her focus is now on finding a way to "reawaken in some way the androgen receptor pathway" to make NEPC tumors more detectable and treatable.

"Our initial observation working with a kinase (an enzyme needed for certain cell processes) called atypical protein kinase C was surprising," she said. "The tumors were completely lacking the presence of this protein; typically tumors show high amounts of this kinase."

She thinks this discovery may lead to a new treatment, one that can make this cancer vulnerable to anti-androgen therapy again.

Early detection is best defense

"In general, for prostate cancer, there are two big risk factors," said Dr. Sven Wenske, urologist and assistant professor of urology at Columbia University Irving Medical Center in New York. "One is ethnicity. For example, African-American men have a significantly higher risk of developing prostate cancer than white men. The other one is a family history of prostate cancer, particularly in a father or paternal uncle, paternal grandfather, or brothers, especially when the disease in those relatives occurred at a younger age."

"However, there is nothing a man can do to prevent prostate cancer," Wenske told Healthline. "Early detection is key. And, while there is a lot of controversy about using PSA as a prostate cancer screening marker,

patients, especially those at higher risk, should certainly seek out a urologist who will perform an 'intelligent' prostate cancer screening."

Intelligent screening involves testing for biomarkers, besides PSA, which can improve screening accuracy.

Wenske said this is because "PSA can be influenced by many factors, so instead of looking at PSA as a set number, but rather indicates the risk of cancer over a continuum. For example, some men with a PSA level below 4 ng/ml could be abnormal, but in other patients a PSA greater than 4 ng/ml could be acceptable."

He explained that additional tests can be helpful in deciding who should undergo a prostate MRI followed by a prostate biopsy to understand which patient has significant prostate cancer that requires treatment.

"If localized prostate cancer is detected and treated early, the success with that is very good," Wenske said.

The bottom line

Prostate cancer, when caught early, can be cured. Powerful new treatments called anti-androgen therapy will stop tumor growth and even shrink them.

But, this same therapy can create treatment-resistant prostate cancer that will spread.

New research has found how this cancer becomes resistant. It may point the way to new anti-androgen treatments that make the disease treatable again.

How we reviewed this article:

HISTORY

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Current Version

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