Research uncovers additional treatment option in prostate cancer

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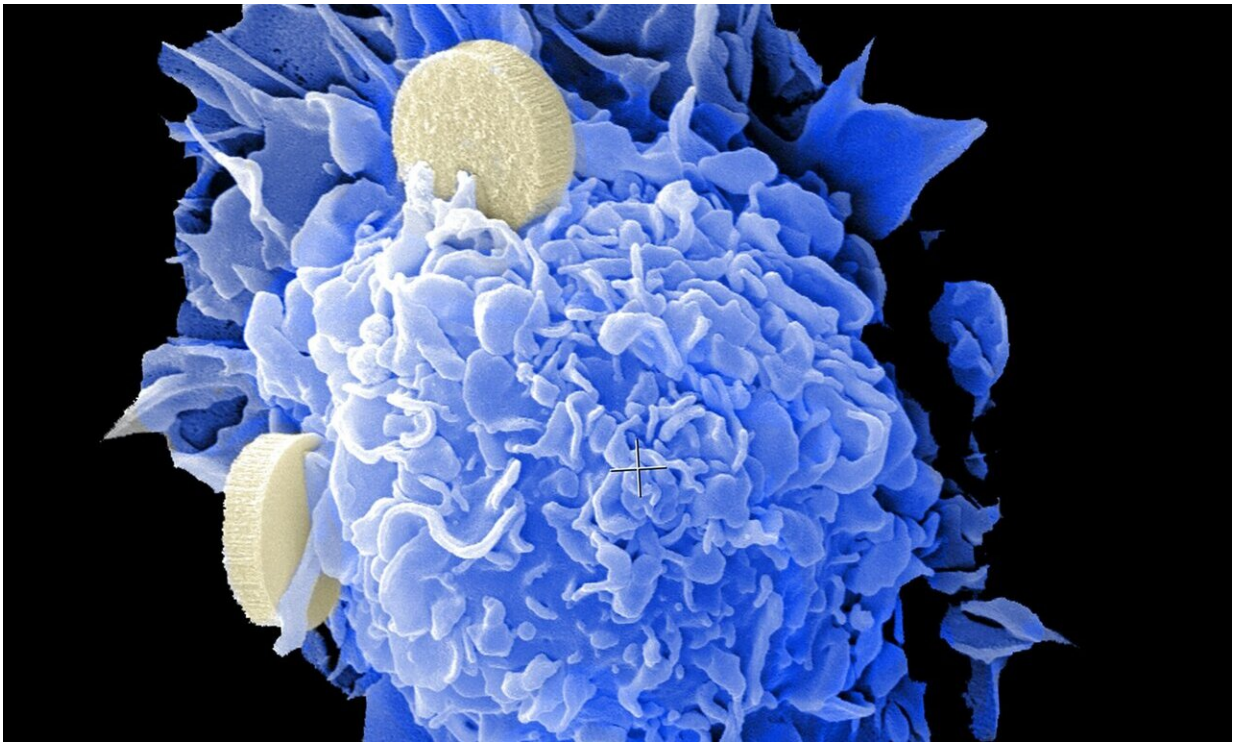

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The standard treatment for advanced metastatic prostate cancer (PCa) is androgen deprivation therapy (ADT). And even if this is efficient in the short term, 1/3 of PCa will become resistant to ADT and develop castration-resistant prostate cancer. A new study, by Karolinska Institutet and others, shows that estrogen receptor β (ERβ) agonists together with

ADT could be considered useful in the treatment.

Prostate cancer is one of the most common cancers and the fifth leading cause of deaths in cancer in men. Androgen deprivation therapy (ADT) is the use of hormones to cause chemical castration and is the usual treatment of metastatic prostate cancer (PCa). And even if this is an efficient way to treat PCa in the short term, some will build up a resistance to this treatment and develop castration-resistant prostate cancer (CRPC). So even if this will increase the number of patients surviving fatal prostate cancer, the effect is temporary and there is a need for alternatives.

ERβ is a tumor suppressor whose expression is lost as PCa progresses and its role in PCa treatments and prevention has been investigated for more than 20 years. This loss limits the use of ERβ agonists for treatment of advanced PCa. But in a new study published in *PNAS*, by Karolinska Institutet, University of Houston, University of Texas MD Andersson Cancer Center and Barmherzige Schwestern Hospital, it is shown that the nuclear transport of epidermal growth factor receptor (EGFR) could be targeted for treatment of PCa with ERβ agonists.

Preventing EGFR nuclear translocation in PCa

Immunochemical staining of sequential sections in tissue arrays indicated that ERβ was expressed in both luminal and basal cells. But the androgen receptor (AR) was only expressed in luminal epithelial cells and not in the basal cells. This is the reason why ADT can prevent the spread of AR-positive cancer cells but has no effect on basal cells.

The researchers found that treatment with the medicine finasteride was related with increased EGFR nuclear translocation, but in men treated with finasteride plus ERβ agonist, isoflavone, there was very little nuclear EGFR. Hence, they suggest that ERβ agonists, by preventing

EGFR nuclear translocation in PCa, might be useful in avoiding the development of tyrosine kinase driven cancers.

"This study provides further evidence that ERβ agonists may be a good medicine against certain forms of prostate cancer," says Professor Jan-Åke Gustafsson at the Department of Biosciences and Nutrition, KI. "This is a line of research that we intend to continue working with," he continues.

More information: Wan-fu Wu et al. Estrogen receptor β and treatment with a phytoestrogen are associated with inhibition of nuclear translocation of EGFR in the prostate, *Proceedings of the National Academy of Sciences* (2021). DOI: 10.1073/pnas.2011269118

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