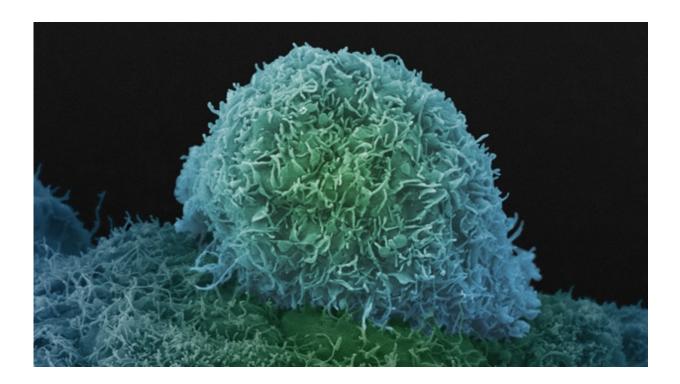


New role for prostate cancer protein could lead to better diagnosis and treatment

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A prostate cancer cell. Credit: LRI EM unit

US scientists studying how prostate cancer cells grow say they've discovered a new role for a protein previously known to be involved in repairing damaged DNA.

The protein DNA-PK – first shown to repair DNA damage in the 1990s by UK scientists – has now been shown to be involved in regulating the



activity of genes involved in cancer spread.

According to study leader Dr Karen Knudsen, from the Sidney Kimmel Cancer Centre, her team's results "strongly suggest" that DNA-PK plays an important role in prostate cancer spread.

"And high levels of DNA-PK could predict which early stage tumours may go on to metastasise [spread]," she added.

Using a variety of laboratory techniques, her team showed that disrupting DNA-PK's activity inside growing <u>prostate cancer cells</u> altered the levels of other key molecules that regulate cell movement, and slowed down the <u>cancer cells</u>' ability to spread.

They also found higher levels of the protein in tumour samples taken from men whose prostate cancer went on to spread.

But UK experts cautioned that more work was needed to build on these findings, which are published in the journal *Cancer Cell*.

Dr Alan Worsley, Cancer Research UK's senior science communications officer, said: "DNA-PK is an important molecule in cancer, and this fascinating research suggests that alongside its well-understood role in DNA repair, it may play a role in the growth and spread of <u>prostate</u> <u>cancer</u>.

"But there's a lot of work ahead to work out exactly how these pieces of the puzzle fit alongside what else we know about how cancer spreads, let alone whether developing drugs to target DNA-PK could be a useful strategy to help patients with the disease."

Cancer Research UK's Professor Steve Jackson, from Gurdon Institute in Cambridge, initially identified the protein's DNA repair functions and



also showed it was possible to target it with drugs. He said the findings were "certainly very intriguing".

"Because of its involvement in DNA repair processes, DNA-PK has already been the subject of drug discovery efforts in industry and academia, with several compounds being reported that interfere with its function."

The US trial team are now planning a new clinical trial of a drug that targets DNA-PK. The drug, code-named CC-115, disrupts both DNA-PK and another cancer-driving molecule, and is already in early-stage testing in the US.

"This new trial will provide some insight into the effect of DNAP-PK inhibitors as anti-tumour agents," said Dr Knudsen.

"Given the role of DNA-PK in DNA repair as well as control of tumour metastasis there will be challenges, but this discovery unveils new opportunities for preventing or treating advanced disease," she added.

More information: "DNA-PKcs-Mediated Transcriptional Regulation Drives Prostate Cancer Progression and Metastasis." *Cancer Cell*, 28 (1), 97-113 DOI: 10.1016/j.ccell.2015.06.004

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