Prostate cancer advance could improve treatment options

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Researchers at the University of East Anglia have made an important advance in understanding genetic changes associated with terminal prostate cancer.

Findings published today in the *British Journal of Cancer*, and funded by the Association for International Cancer Research (AICR), show how a genetic mutation in untreated patients is linked to aggressive cancer later in life. It was previously thought that the mutation only occurred in response to therapy.

The research highlights why relapses could occur in some men following hormone therapy. And it could help identify those patients that will develop fatal prostate cancer much earlier for life-extending therapy.

Prostate cancer is the most common cancer in men in the UK, with more than 40,000 new cases diagnosed every year. Treatment options for patients diagnosed with early stage prostate cancer vary from "watchful waiting" to hormone-withdrawal therapy, radiotherapy or surgery.

Additional tests for indicators of aggressive cancer are necessary to help categorise patients so that those with a low-risk of the disease spreading can avoid unnecessary treatment, and those diagnosed with a high-risk can be targeted for more aggressive first line therapy.

Hormone-withdrawal therapy often results in a dramatic remission, however the disease invariably relapses with a resistant form of the

cancer. A third of these are due to an increase in copy number of a particular gene called the 'androgen receptor'. The gene is on the X-Chromosome and so there is normally only one copy of this gene present in men. Prostate cancer thrives on male hormones, and one way that they develop to grow better is to increase the number of copies of the androgen receptor gene. This also enables the cancer to resist therapy.

Lead researchers Dr Jeremy Clark and Prof Colin Cooper from UEA's school of Biological Sciences carried out the research at the Institute of Cancer Research, London, and at UEA.

Dr Clark said: "By the age of 60, the majority of men will have signs of prostate cancer. However, only a small proportion of men will die of the disease. The question is - which of these cancers are dangerous and which are not? Deciding which cancers are going to progress and kill the patient is key to effective patient treatment."

"Prostate cancer thrives on male hormones, and cutting the supply of hormones to the cancer is a main avenue of therapy. Prostate cancer only kills the patient when it becomes immune to these therapies. A third of these killer cancers are immune to therapy because they have boosted the number of male hormone receptor (AR) genes in their DNA. This gene boosting, also known as amplification, has been thought to be a response of the tumour to the hormone reduction therapy itself.

"Our research has shown that an early form of this hormone-gene boosting is present in a number of prostate cancers that have never been treated with hormone reduction therapy. We think that it is these cancers that will grow and kill the patient.

"This discovery can be used to identify these killer cancers in patients much earlier than is currently possible. Patients could then be selected for more aggressive therapy before the cancer has developed full

immunity."

The research team looked at biomarkers from almost 600 patients prior to hormone-withdrawal therapy. But the method of identification used was labour intensive and time consuming. Developing ways of identifying patients for early therapeutic intervention will be key to implementing this discovery in the clinic. The research team are currently looking at more rapid ways of identifying patients that will develop aggressive cancer.

More information: 'Focal amplification of the androgen receptor gene in hormone-naïve human prostate cancer' is published in the *British Journal of Cancer*. www.nature.com/bjc/journal/vao … full/bjc201413a.html

Provided by University of East Anglia