World-first tissue study could re-shape future of advanced prostate cancer treatment

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The first-ever comprehensive study of prostate cancer tissue has revealed a completely new gene network driving the disease in patients who have stopped responding to standard hormone treatment, according to Cancer Research UK research published today in *Cancer Cell*.

Surgeons at the Cancer Research UK Cambridge Research Institute, at the University of Cambridge studied tissue samples from men with prostate cancer. They discovered that a protein called the androgen receptor fuels advanced prostate cancer by switching on genes previously not linked with the disease. These findings reveal potential new drug targets and markers that could be used to monitor progression of the cancer.

Prostate cancer is mainly driven by androgens – the male sex hormones

– which send messages through the androgen receptor into the cells and tissues. When these messages are faulty they can trigger cancer cell division.

Standard treatment for prostate cancer includes blocking these androgens. But some men become resistant to the drugs – developing what is known as castrate-resistant prostate cancer.

Previous cell studies have shown that the androgen receptor attaches to and 'switches on' specific genes to drive cancer.

But this tissue study reveals, for the first time, that when androgen is absent from the bloodstream, the androgen receptor continues to fuel the disease by switching on a completely different gene set. This includes genes associated with the production of glucose and fat.

Study author, Naomi Sharma, Urology Academic Registrar at Addenbrooke's Hospital based at the Cancer Research UK Cambridge Research Institute, said: "This is the first comprehensive tissue study of its kind and shines a new light on the biology of prostate cancer.

"Our understanding so far comes from studies in cells grown in the laboratory. In this sophisticated study using samples directly from patients, we've uncovered a much more complex network of cell messages. These messages switch on a completely different set of genes that continue to drive the disease in men for whom standard hormone treatments have stopped working.

"These important findings provide fresh targets for the development of new drugs to treat advanced stages of prostate cancer, and new 'flags' to help doctors track the progression of the disease in patients."

Up to 41,000 men in the UK are diagnosed with prostate cancer each

year – the most common cancer in UK men – and around 10,700 men die from the disease each year.

Professor Malcolm Mason, Cancer Research UK's prostate cancer expert, said: "This fascinating research reframes our understanding of how the androgen receptor works – painting a very different picture of how it drives cancer.

"I run clinical trials aiming to help men with prostate cancer so I'm keenly aware of the need to find new ways for us to deal with the disease.

"We helped to develop abiraterone – an important new drug for treating men with advanced disease. And it's thanks to the generosity of our supporters, that we're able to fund cutting-edge research like this, which is helping us work towards a day when cancer is cured."

More information: Sharma et al. The androgen receptor induces a distinct transcriptional program in castration resistant prostate cancer in man. *Cancer Cell*.

Provided by Cancer Research UK

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