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Scientists solve key piece of prostate cancer puzzle

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Cancer Research UK scientists have revealed a completely new route by which male androgen hormones fuel the growth of prostate cancer, raising the prospect that existing drugs could be used to treat the disease.

Prostate cancers are often treated with hormone therapies that target the androgen receptor (AR) – a large protein that switches on signals telling the cell to divide, and which can become overactive in prostate cancer cells.

AR relies on interactions with several other proteins, such as HSP90 and p23, which help fold it into its active form.

Previously it was thought that p23 and HSP90 work together to activate AR, but this latest research – funded by Cancer Research UK and the Association for International Cancer Research – shows that p23 also increases activity of the AR independently.

Crucially this means that drugs to block p23 could be effective at treating prostate cancers that have become resistant to HSP90 inhibitors – which are currently being trialled in breast and prostate cancers.

The findings are published in *Molecular Endocrinology*.

Study leader, Dr Charlotte Bevan, from the Department of Surgery and Cancer at Imperial College London, said: “Cell signals from the androgen receptor (AR) drive many prostate cancers and our team is part

of an ongoing international effort to find new drug targets that can potentially disable this key protein.

“Previously it was thought that HSP90 and p23 went hand in hand, so we were surprised to find that p23 was also able to boost the activity of the androgen receptor even when we used a modified form that was unable to bind HSP90.

“Excitingly, drugs that block p23 such as Celastrol, which is derived from a plant used in Chinese medicine, have shown early promise in treating several diseases, such as arthritis and asthma, meaning this research is already a step closer to the clinic. The next stage will be to test the effects of such drugs on prostate cancer cells in the lab.”

The researchers used antibodies specifically designed to target p23 to show that levels of the protein are higher in the nucleus of prostate cancer cells compared to normal cells. They also used a modified form of p23, unable to bind HSP90, to show that p23 can act independently of HSP90 and does not necessarily need the protein to interact with the AR.

Dr Julie Sharp, senior science information manager at Cancer Research UK, said: “These results provide an alternative route by which scientists could potentially target prostate cancer by halting AR activity. What’s more, p23 has a much more defined role in the cell than HSP90, meaning that drugs that target it could potentially have fewer side effects for patients than HSP90 inhibitors. We hope these findings will lead to better treatment options for men with prostate cancer.”

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