

A potential new target for treatment of hormone refractory prostate cancer

6 April 2009

A new study identifies a protein that modifies the androgen receptor (AR) and influences its ability to regulate target genes linked with the progression of prostate cancer. The research, published by Cell Press in the April 7th issue of the journal *Cancer Cell*, may also drive creation of new strategies for the treatment of advanced prostate cancer that no longer responds to traditional anti-hormone therapies.

The AR is an important mediator for the development and progression of [prostate cancer](#), including the progression to the aggressive and often lethal androgen-independent form of the disease. "Androgen ablation therapy is the most common treatment for advanced prostate cancer," offers senior study author, Dr. Yun Qiu from the University of Maryland School of Medicine. "However, many patients inevitably develop deadly recurrent cancers, which no longer respond to androgen blockade and are resistant to current therapy."

To better understand mechanisms associated with advanced prostate cancer, Dr. Qiu and colleagues performed a screen designed to search for proteins that interact with the AR in hormone-refractory [prostate cancer cells](#). The researchers identified RNF6 as an AR associated protein and demonstrated that RNF6 induced ubiquitination of the AR and promoted AR transcriptional activity. Ubiquitination is a common protein modification that mediates a diverse range of cellular activities. One of the best known functions of ubiquitination is to promote protein degradation. However, ubiquitination of AR by RNF6 appeared to have a stabilizing effect on AR protein.

Importantly, inhibition of RNF6 or interference with ubiquitination of AR altered expression of a specific group of AR target genes and abrogated recruitment of AR and its required coactivators to androgen-responsive regulatory regions in these genes. The researchers went on to show that

expression of RNF6 was increased in human prostate cancer tissues that do not respond to androgen ablation and is required for prostate tumor growth under androgen depleted conditions.

Taken together, the findings implicate RNF6 as an important regulator of AR transcriptional activity. "Our work suggests that ubiquitination of AR, and possibly other transcription factors, may function as the scaffold for cofactor recruitment to modulate transcriptional activity and specificity," concludes Dr. Qiu. "Targeting components of the ubiquitination machinery, such as RNF6, may potentially be effective in treatment of advanced prostate cancer."

Source: Cell Press ([news](#) : [web](#))

APA citation: A potential new target for treatment of hormone refractory prostate cancer (2009, April 6) retrieved 24 September 2022 from <https://medicalxpress.com/news/2009-04-potential-treatment-hormone-refractory-prostate.html>

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