TECHNOLOGY

Novel Alternatively Spliced Human Androgen Receptor Variants as Biomarkers for Prostate Cancer

OVERVIEW

Prostate cancer is the second leading cause of cancer death among men in western countries. Patients with advanced prostate cancer initially benefit from androgen ablation therapy which leads to temporary remission of the tumor due to apoptosis of androgen-sensitive tumor cells. However, the recurrence of androgen-independent tumors is inevitable for most patients and renders the conventional hormone therapy ineffective. It has, therefore, become a focus of intensive study to understand the mechanisms underlying progression of hormone refractory prostate cancer. Validation of tumor progression markers is an essential component for developing effective prostate cancer treatment strategies. Researchers at the University of Maryland, Baltimore have discovered novel alternately spliced isoforms of the androgen receptor, which are constitutively active and not affected by androgens or by standard anti-androgen drugs used to treat prostate cancer. UMB researchers validated the AR3 splice variant as a potential prognostic marker, correlating AR3 expression in hundreds of samples from prostate cancer patients with the clinical outcome for those patients. Another novel AR splice variant, designated as AR8, is up-regulated in castration-resistant prostate cancer cells, and it's structurally different from other known splice variants because it lacks a DNA binding domain. UMB researchers demonstrated that the membrane-associated AR8 isoform may contribute to castration resistance by potentiating AR-mediated proliferative and survival responses to hormones and growth factors.

APPLICATIONS

Target for development of new drugs to treat prostate cancer. Prognostic biomarker for prostate cancer which may be used for optimizing patient treatment strategy.

ADVANTAGES

This variant of the androgen receptor presents a novel target for development of effective prostate cancer treatments. Blocking genetic expression of AR3 in mouse xenograft models reduced tumor growth. As a biomarker, promises to enhance patient treatment strategy for more effective therapy of recurrent prostate cancer.

STAGE OF DEVELOPMENT

-In human prostate tissue samples, AR3 was shown to be much more prevalent in patients with hormone resistant cancer, and was shown to be a significant predictor of tumor recurrence. -In prostate cancer cells, AR3 was not inhibited by currently available anti-androgen drugs such as casodex.

R&D REQUIRED

Specific development directed to use as biomarker or therapeutic target.

LICENSING POTENTIAL

UMB seeks development partner for licensing and/or sponsored research.

CONTACT INFO

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Additional Information

INSTITUTION

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PATENT STATUS

U.S. Patent 8,133,724, issued March 13, 2012; and U.S. Patent 8,841,422, issued September 23,2014

LICENSE STATUS

Available for licensing

CATEGORIES

- Diagnostics

INVESTIGATOR(S)

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EXTERNAL RESOURCES

- Novel membrane-associated androgen receptor splice variant potentiates proliferative and survival responses in prostate cancer c
- A new trick of an old molecule: androgen receptor splice variants taking the stage?!
- Androgen receptor splice variant AR3 promotes prostate cancer via modulating expression of autocrine/paracrine factors

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