Despite depleting circulating levels of androgens via ADT, tumor progression is often associated with prostate cancer (PCa) being the second leading cause of cancer-related mortality among men in Western societies, and it affects approximately 1 in every 10 male individuals. Prostate cancer is mediated by the androgen receptor (AR) signaling pathway through its upstream activation and denaturation. Mutations, amplification, and posttranslational modifications of AR all lead to prostate tumorigenesis. The principle treatment for locally advanced and metastatic PCa is androgen deprivation therapy (ADT). While initially enabling regression of the disease for the majority of patients, as shown by a decrease in prostate-specific antigen (PSA), the disease begins to progress after 2-3 years. This advanced state of lethality, with a mean survival time of only 16-18 months, is known as castrate-resistant prostate cancer (CRPC) and comes with a poor prognosis and high mortality. The disease begins to progress after 2-3 years. This advanced state of lethality, with a mean survival time of only 16-18 months, is known as castrate-resistant prostate cancer (CRPC) and comes with a poor prognosis and high mortality.

Mutations, amplification, and posttranslational modifications of AR all lead to prostate tumorigenesis. One of the major contributing factors is the expression of AR-splice variants. Recent evidence points to the existence of alternatively spliced forms of AR mRNAs, which encode receptors devoid of the ligand-binding domain (LBD) but retain the DNA binding domain (DBD). This allows for increased nuclear localization of AR resulting in unregulated transcription and therapy-resistant prostate cancer.

**Hypothesis**

- Given that AR-V7 retains the DBD region of AR, we hypothesize that ARD1 overexpression may act as a co-activator of AR-V7 by acetylating the DBD domain. This allows for increased nuclear translocation, target gene expression, and ultimately CRPC.

**Methods**

**ARD1 Acetylation of AR-V7 in Prostate Cancer**

**Fougereousse J, Qian C, Guo J, and Liu W**

Stanley S. Scott Cancer Center, Louisiana State University Health Sciences Center, New Orleans, LA, USA.

**Introduction**

- Prostate cancer (PCa) is the second leading cause of cancer-related mortality among men in Western societies, and it affects approximately 1 in every 10 male individuals. Prostate cancer is mediated by the androgen receptor (AR) signaling pathway through its upstream activation and denaturation. Mutations, amplification, and posttranslational modifications of AR all lead to prostate tumorigenesis.

- The principle treatment for locally advanced and metastatic PCa is androgen deprivation therapy (ADT). While initially enabling regression of the disease for the majority of patients, as shown by a decrease in prostate-specific antigen (PSA), the disease begins to progress after 2-3 years. This advanced state of lethality, with a mean survival time of only 16-18 months, is known as castrate-resistant prostate cancer (CRPC) and comes with a poor prognosis and high mortality. The disease begins to progress after 2-3 years. This advanced state of lethality, with a mean survival time of only 16-18 months, is known as castrate-resistant prostate cancer (CRPC) and comes with a poor prognosis and high mortality.

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**Arrest Defective-1 protein (ARD1)**

- AR-V7 is an androgen-responsive that is overexpressed in prostate cancer.

**AR-V7**

- AR-V7 retains the DBD region of AR, which leads to prostate tumorigenesis.

**In Vitro Acetylation**

- In vitro acetylation of AR-V7 DBD demonstrates auto-acetylation.

**Conclusion**

- In vitro acetylation of AR-V7 DBD demonstrates auto-acetylation.
- Further investigation reveals that, without the 16 amino acid C-terminal region, auto-acetylation still occurs.

**Future Directions**

- Develop Ab specific for AR-V7-AC to determine if an increase in AR-V7 acetylation correlates with CRPC progression.