

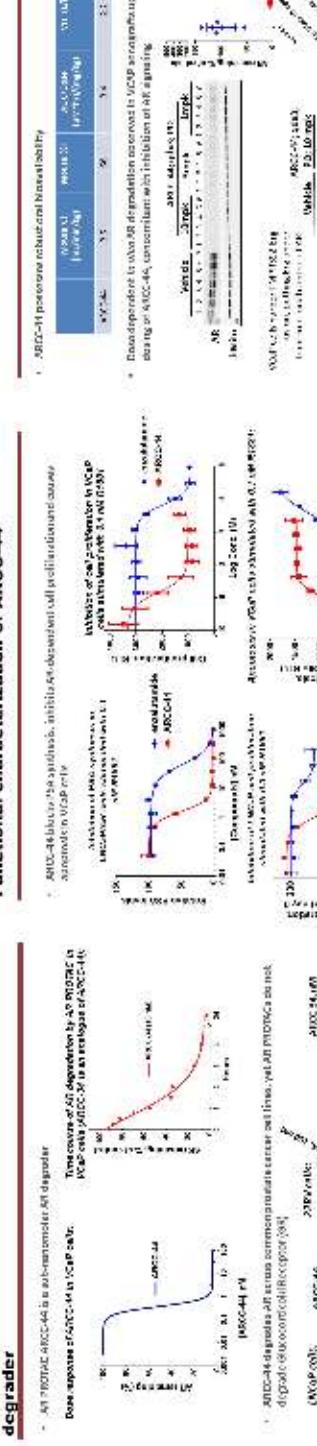
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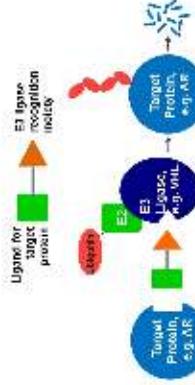
Abstract

Background: ARCC-44 is an orally-available, small molecule antagonist of the androgen receptor (AR) that selectively targets the extracellular domain of the AR. It has been shown to induce AR degradation, reduce AR expression, and inhibit AR signaling in prostate cancer cells. In this study, we report a comprehensive characterization of ARCC-44 and its potential as a therapeutic agent. Results: ARCC-44 is a potent, orally-available, AR antagonist that selectively degrades AR protein in cells expressing AR. It has no effect on other nuclear receptors, including PGR, VDR, TRα, TRβ, and RARα. ARCC-44 is selective for the extracellular domain of the AR and can induce proteasomal degradation of AR protein, reduce AR expression, and inhibit AR signaling. Conclusion: ARCC-44 is a potent, orally-available AR antagonist that selectively degrades AR protein, reduces AR expression, and inhibits AR signaling.

Characterization of ARCC-44 – a potent AR PROTAC degrader

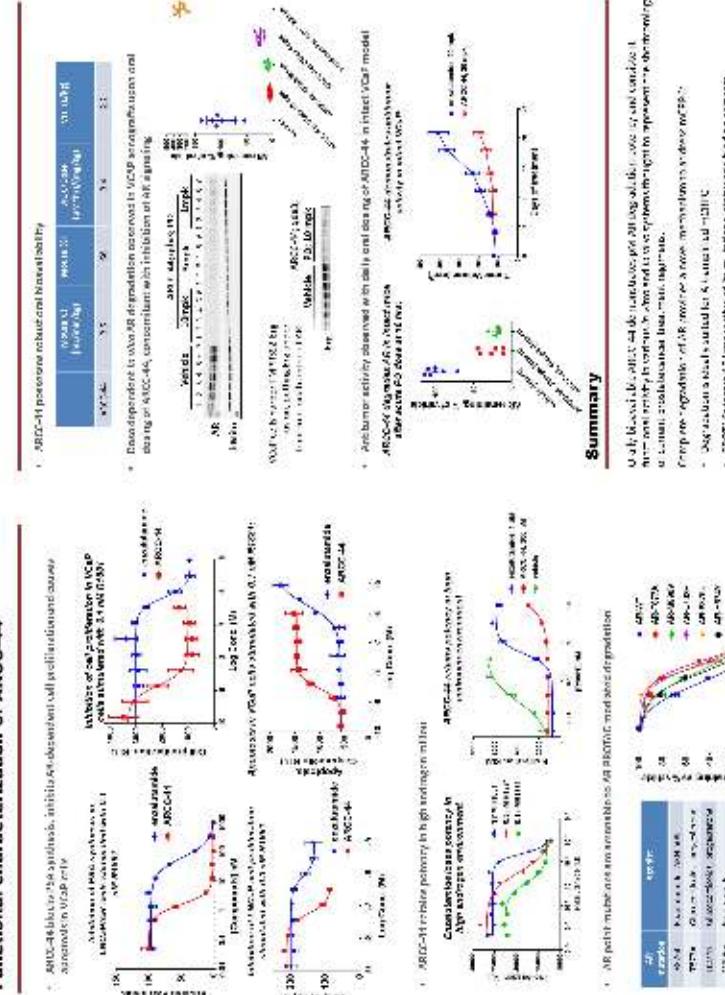


PROTAC: PROteolysis Targeting Chimeras



Second: Androgen receptor antagonist
1. PROTAC with target specificity
2. Androgen receptor inhibitor
3. Androgen receptor antagonist

Functional characterization of ARCC-44



- Androgen receptor antagonist
- Androgen receptor inhibitor
- Androgen receptor antagonist

Second: Androgen receptor antagonist
1. PROTAC with target specificity
2. Androgen receptor inhibitor
3. Androgen receptor antagonist

- Androgen receptor antagonist
- Androgen receptor inhibitor
- Androgen receptor antagonist

Summary

- Oral ARCC-44 exhibits potent AR degradation in subcutaneous and prostate cancer cells.
- ARCC-44 inhibits AR-induced proliferation in LNCaP cells, but not in other cancer cells.
- ARCC-44 is a potent, orally-available, AR antagonist that selectively degrades AR protein.
- ARCC-44 is selective for the extracellular domain of the AR.
- ARCC-44 induces AR degradation in cells expressing AR.

Acknowledgments

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