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Targeting the turnover of oncoproteins as a new avenue for therapeutics development in castration-resistant prostate cancer

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**Abstract**

The current therapeutic armamentarium for castration-resistant prostate cancer (CRPC) includes second-generation agents such as the Androgen Receptor (AR) inhibitor enzalutamide and the androgen synthesis inhibitor abiraterone acetate, immunotherapies like sipuleucel-T, chemotherapies including docetaxel and cabazitaxel and the radiopharmaceutical radium 223 dichloride. However, relapse of CRPC resistant to these therapeutic modalities occur rapidly. The mechanisms of resistance to these treatments are complex, including specific mutations or alternative splicing of oncogenic proteins. An alternative approach to treating CRPC may be to target the turnover of these molecular drivers of CRPC. In this review, the mechanisms by which protein stability of several oncoproteins such as AR, ERG, GR, CYP17A1 and MYC, will be discussed, as well as how these findings could be translated into novel therapeutic agents.