

Deciphering AR genomic rearrangements in prostate cancer

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Background: Molecularly targeted therapies for advanced prostate cancer include castration modalities that suppress ligand-dependent transcriptional activity of the androgen receptor (AR). However, persistent AR signaling undermines therapeutic efficacy and promotes progression to lethal castration-resistant prostate cancer (CRPC), even when patients are treated with potent second-generation AR-targeted therapies abiraterone and enzalutamide.

Methods: In this study, we developed an integrated structural variation (SV) detection pipeline which leverages multiple SV signals for studying the spectrum of AR gene rearrangements with high accuracy and resolution.

Results: With our analysis, we have identified diverse AR genomic structural rearrangements (AR-GSRs) as a class of molecular alterations occurring in one third of CRPC-stage tumours.

Conclusions: Overall, these data indicate that AR gene rearrangements are frequent, yet non-recurrent, in CRPC patients. This knowledge supports future studies designed to understand the impact of these AR gene rearrangements on AR mRNA and protein expression patterns, as well as patient responses to AR-targeted therapy.

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