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Phosphorylation of Androgen Receptor Serine 81 is Associated with its Reactivation in Castration-Resistant Prostate Cancer

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Abstract

Phosphorylation of serine 81 (pS81) in the N-terminal transactivation domain of the androgen receptor (AR) has been linked to its transcriptional activation in prostate cancer (PCa) cell lines, but *in vivo* studies have been limited. Moreover, the role of pS81 in the reactivation of AR when tumors relapse after androgen deprivation therapy (castration-resistant prostate cancer, CRPC) has not been determined. In this study we validate a pS81 antibody for immunohistochemistry (IHC) and show it yields strong nuclear staining in primary PCa clinical samples and in the VCaP PCa xenograft model. Moreover, this staining was decreased at 7 days post-castration in VCaP xenografts, coinciding with markedly decreased AR transcriptional activity. Staining with the pS81 antibody then was restored when the VCaP xenografts relapsed, which was associated with restoration of AR transcriptional activity. Significantly, analysis of CRPC clinical samples, including tumors that had progressed during treatment with abiraterone, showed strong nuclear staining with the pS81 antibody. Together these findings indicate that AR reactivation in CRPC is associated with S81 phosphorylation, and suggest that IHC for pS81 may be useful as a biomarker of AR activity in CRPC.

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