The androgen receptor (AR) and the NF-kappaB/IKK signaling pathway are two transcriptional systems shown to be important for the initiation and progression of prostate carcinoma (PCa). Furthermore, recently published studies imply a cross-talk between these two transcriptional systems. In order to define this cross-talk, we impaired the NF-kappaB/IKK system by using either pharmaceutical inhibitors or siRNAs specific for IKK and NF-kappaB proteins. Results from these studies imply that IKK inhibitors might be a useful tool for the therapy of PCa.
Prostate cancer (PCa) is the most common cancer diagnosed in elderly men and the second leading cause of cancer-related death in the western world. The development and progression of PCa is initially androgen dependent but castration resistant tumours frequently occur after hormone ablation therapy. A reason for that is a dysregulation of androgen receptor (AR) cofactors. Cofactors are proteins that interact with nuclear receptors and either upregulate (coactivators) or downregulate (corepressors) the transcriptional activity of their target genes. These cofactors play a crucial role in tumour progression and development of castration resistant tumours. We investigated the corepressors NCoR (nuclear receptor corepressor) and SMRT (silencing mediator of retinoic acid and thyroid hormone receptor) in prostate and non-prostate cells using amongst others transactivation studies and mammalian two hybrid assays. The corepressors are localized exclusively in the nucleus, even in the absence of hormone (Fig. 2).

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