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Role of androgen receptor in epithelial to mesenchymal transition (EMT) in prostate cancer cells

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Epithelial to mesenchymal transition (EMT) plays a vital role in cancer metastasis. Androgen and its receptor have not been investigated extensively for their role in the EMT regulation in prostate cancer (PCa). Moreover, some reports suggest that androgens activate EMT in PCa while others have demonstrated EMT activation on attenuation of androgen receptor (AR) expression in PCa and on androgen deprivation in mouse prostate. Thus, data on the role of androgenic stimuli in the EMT regulation in PCa are ambiguous. Therefore, this study was undertaken to delineate whether modulation in the levels of AR alters the invasiveness and phenotypic characteristics of prostate cancer cells. Microarray analysis of AR silenced LNCaP cells revealed differential expression of EMT associated genes such as ZEB2, TWIST, Wnt/ β catenin, and TCF4. A significant ($p < 0.05$) decrease was observed in ZEB2 expression in AR silenced cells while its expression was found to be significantly up-regulated after androgen stimulation of androgen-dependent cells. This was suggestive of a facilitatory role of AR in the regulation of ZEB2 expression in androgen-dependent cells. Reduced levels of ZEB2 in the AR silenced cells led to a significant ($p < 0.05$) reduction in the invasiveness of androgen-dependent cells. Forced expression of AR in PC3 and DU145 cells led to a decrease in the expression of ZEB2. This caused a decline in their invasiveness and migratory abilities and an up-regulation of the levels of E-cadherin. Transfection with ZEB2 cDNA construct restored their abilities to migrate and invade. Further, a significant increase in the levels of ZEB2 and AR was also observed in PCa compared to BPH human tissues. AR therefore acts as an EMT regulator and involves ZEB2 as an intermediary factor in PCa. It may be inferred that AR sustenance in androgen independent cells may help in regulating PCa metastasis.

Biography

Sheeba Jacob is pursuing her PhD from National Institute for Research in Reproductive Health, Mumbai University, India. Her work involved understanding the role of androgen receptor in the regulation of telomerase (hTERT) in prostate cancer cells. She has five papers to her credit and has also presented her work at various conferences. She has also been awarded Department of Atomic Energy-Junior Research Fellowship and Indian Council of Medical Research-Senior Fellowship during her PhD.

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