

Androgen Deprivation Therapy Enhances Cancer Stem Cell Population in Prostate Cancer

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Prostate cancer is the second most common cancer in the United States and the second leading cause of death in men. Androgen-Deprivation Therapy (ADT) is a current treatment modality for advanced-stage prostate cancer, but it remains controversial. More than 30% of patients who have undergone ADT show signs of cancer recurrence and/or androgen-independent disease. Some adverse effects of ADT includes hot flashes, metabolic disorders, alteration in bone mineral density, cardiovascular problems, and sexual dysfunction. Cancer stem cells (CSCs) are a small percentage of cells in a tumor that reinitiates tumor growth. SOX2 is a transcription factor which with high expression may indicate poor prognosis through increased drug resistance and metastasis. OCT4 is the core transcription factor for maintaining pluripotency and is related to tumorigenicity and malignancy. We hypothesize that ADT alters the phenotype of cancer cells to cancer stem cell-like features with higher expression of SOX2 and OCT4. We determined whether ADT results in enrichment of CSCs with higher expression of SOX2 and OCT4. SOX2 and OCT4 expression was determined in subset of patients with and without ADT by immunohistochemistry (IHC). IHC slides were assigned an immunoreactive score (IRS) using the percentage of positive cells and intensity of the color reaction. Additional experiments utilized C4-2B-ENZU cells generated by growing C4-2B cells in 5-20 μ M of ENZU over 60 days and maintained in 5 μ M ENZU in the cell culture medium and androgen-responsive human prostate cancer LNCaP cells to assess SOX2 and OCT4 levels by Western blotting. The IRS scores for SOX2 were 1.635 for non-ADT compared to 3.040 for ADT with higher staining for SOX2 and a higher percentage of positive cells. The IRS scores for OCT4 were 1.733 for non-ADT compared to 1.914 for ADT showing a modest difference in the expression of OCT4 expression. In the Western blot data, expression of OCT4 was higher in the LNCaP-ENZU treated cells and the SOX2 expression is higher in the C4-2B ENZU treated cells. This indicates that the expression of CSC markers increases in patients undergoing ADT protocol. Further studies are required to determine the involvement of CSCs in CRPC acquisition as well as the pathways and factors contributing to its expansion in response to ADT.