Combinatorial strategy of epigenetic and hormonal therapies: A novel promising approach for treating advanced prostate cancer

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Abstract

Aims

Estrogens act as key factors in prostate biology, cellular proliferation and differentiation as well as cancer development and progression. The expression of estrogen receptor (ER)-ϐ appears to be lost during prostate cancer progression through hypermethylation mechanism. Epigenetic drugs such as 5-aza-2¶-deoxycytidine (5-AZAC) and Trichostatin A (TSA) showed efficacy in restoring ERϐ expression in prostate cancer cells. This study was designed to explore the potential anti-carcinogenic effects resulting from re-expressing ERϐ1 using 5-AZAC and/or TSA, followed by its stimulation with Diarylpropionitrile (DPN), a selective ERϐ1 agonist, in prostate cancer cell line PC-3.

Main methods

Cells were treated with 5-AZAC, TSA, DPN and their combination. Subsequently, they were subjected to proliferation assays, determinations of ERϐ1 expression, protein levels of active caspase-3, cyclin D1, ϐ-catenin and VEGF.

Key findings

Treatment with these drugs exhibited an increase in ERϐ1 expression to different extents as well as active caspase-3 levels. Meanwhile, a significant reduction in cyclin D1, VEGF and ϐ-catenin levels was achieved as compared to the vehicle control group (pȷ<ȷ0.05). Interestingly, the triple combination regimen led to the most prominent anti-tumor responses in terms of increased apoptosis, reduced proliferation as well as angiogenesis.

Significance

The results support the notion that ERϐ1 acts as a tumor suppressor protein and suggest that sequential ERϐ1 expression and activation can offer significant anti-tumor responses. The study highlights that the strategy of merging epigenetic and hormonal therapies may be beneficial in treating advanced prostate cancer

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