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Upregulated FOXO 1 & 3 down regulate the tumour suppressor HOXB13, HOXB3, CHEK2, SPOP, RB1 genes in prostate cancer

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Introduction & Objectives: Cancer is multifactorial, abnormal proliferation and differentiation of cells of the different tissues in the body. It is second main cause of death around the globe after cardiovascular diseases. Prostate gland is the main male accessory gland involved in sperm growth and lubrication of urogenital tract. Among all the cancer types in males, prostate cancer is the second most diagnosed cancer worldwide. Molecular and genetic players of prostate cancer have already been studied extensively in modern research area. In subcontinent generally and in Pakistan specifically, epigenetics and expression of onco-suppressive/ proto-onco genes in prostate cancer are not extensively studied in recent past. Role of some genes such as, SPOP, RB1, BRCA1, BRCA2, PTEN, HOXB 3, HOXB13, AR and CHECK2 were predicted as tumor suppressor genes in progression of prostate cancer.

Materials & Methods: Current study was designed to identify the potential expression of HOXB13, HOXB3, CHEK2, SPOP, RB1 genes responsible for the translation of onco-suppressor proteins in prostate cancer patients and to elucidate the possible cross talk among backstage pathways likewise Wnt, FOXO1 & 3 and PI3k pathways that resulting in genetic modifications. Biopsy samples of patients were collected from PINUM and ALLIED health care facility of the city after approval of ethical review committee. Samples were subjected to further analysis for histopathology and RNA extraction. Gene expression analysis was performed by following standard protocols of qRT-PCR and Gel-electrophoresis. Data was statistically analyzed through analysis of variance and DMR.

Results: Gene expression analysis results revealed that SPOP, RB1, HOXB3, CHEK2 and HOXB13 genes were significantly down expressed ($P<0.05$) while as, FOXO1 & 3 genes were upregulated in prostate cancer patient samples ($P<0.05$). PI3k pathway cross talk with wnt-beta catenin signaling was also significantly involve in perturbation of onco-suppression ($P<0.05$). Histopathological analysis confirmed the structural disruption of prostate gland and proliferation of epithelial cells in patient samples having grade 1 to grade 5 cancer progression.

Conclusions: We conclude that down regulation of onco-suppressive genes and up-stream FOXO 1 and 3 in response to mutation of Wnt-beta catenin signaling / PI3k pathway lead towards prostate cancer progression and metastasis in elderly patients and some patients of age above 35 with family history of tumorigenesis.