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Topic: Molecular Analysis of FOXO1 and FOXO3 genes
in Indian Breast Cancer Patients
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FINDINGS

FOXO proteins belong to Forkhead box family of transcription factors having a conserved DNA binding domain. These proteins are increasingly considered to represent distinctive cellular targets focused against human cancer in light of their pro-apoptotic effects and capability to lead to cell cycle arrest. FoxOs also can significantly affect normal cell survival and longevity, requiring new treatments for neoplastic growth to modulate novel pathways that integrate cell proliferation, metabolism, inflammation, and survival. FOXO1 and FOXO3 transcription factors are the members of FOXO subfamily and major targets of PI3/Akt signalling, are known to be associated with regulation of metabolic homeostasis. Significant role of PI3/Akt signalling in various cellular processes makes it prime target for investigation and research. PI3/Akt pathway have crucial role in cell survival and growth during carcinogenesis, FOXO1 and FOXO3 are the downstream targets of this pathway. To better understand their role in predisposition of Breast cancer, expression and epigenetic study was conducted in North Indian Female Breast Cancer patients and further stratified analysis was done to evaluate the correlation of risk with various clinicopathological parameters. The present study comprises the evaluation of expression of both genes at mRNA and Protein level and their methylation status at various CpG islands.

Both FOXO1 and FOXO3 genes at mRNA level seems to downregulated in 68 cases out of 127 patients and upregulated in 23 patients. When mRNA expression of both the genes was correlated, statistically significant correlation ($p=0.0001$) was seen between them. Following to mRNA expression studies, protein expression was also evaluated to see if mRNA expression is corroborated with protein level. Moreover, for proper functioning of protein, its sub cellular localization is very crucial to study as it alters the functionality of the protein. To investigate this, Immunohistochemistry technique was used to evaluate the protein expression. It was detected that protein expression of both FOXO1 and FOXO3 very well corroborated with mRNA expression.