Cervical Cancer: One small step towards understanding the riddle

Current study aimed at unfurling the targets of HPV16 E7 protein, both coding and non-coding RNAs, to get a holistic view of the mechanisms involved and to identify suitable genes and pathways that could be therapeutically manipulated for patient cure. Towards this, we have cloned the HPV16 E7 gene in a mammalian expression vector and transfected HPV negative cervical cancer cells, C33A, for E7 expression. Team then isolated RNA from transfected and untransfected cells and performed global RNA seq assay to identify genes that show deregulated expression under the influence of HPV16 E7 by comparing the two datasets.

Previous studies from same laboratory showed that E7 protein can bring about epigenetic changes of certain gene promoters that can upregulate gene expression by relaxation of chromatin structure. Histone modifications such as H3K4me3 and H3K27me3 participate in chromatin relaxation and compaction, respectively. Therefore, we are currently undertaking ChIP experiments, under the same conditions of transfection of C33A cells with E7 and untransfected C33A cells, followed by pull down of DNA employing antibodies against H3K4me3 and H3K27me3, to identify genes that are upregulated or downregulated by such epigenetic alterations of gene promoters, induced by E7. Comparison of such data with the RNA seq data will help to identify characteristic gene sets which are targeted by E7.

Thus, understanding how HPV16 E7 oncoprotein targets other cellular transcripts thereby facilitating cervical cancer pathogenesis by altering gene expression globally will open new therapeutic avenues to modulate their function.

In India, cervical cancer is a major cause of cancer related mortality in women. One of the major causes of cervical cancer development is persistent infection of the cervical mucosal epithelium with oncogenic Human Papillomavirus (mainly HPV type 16/18). HPV genome is noted for its expression of oncoproteins E6 and E7, which are necessary for malignant conversion. The abilities of high-risk HPV E6 and E7 proteins to functionally inactivate the tumor suppressors' p53 and pRB, respectively, have been suggested as mechanisms by which, these viral proteins induce tumors.

For investigations on the pathogenesis of cervical cancer, the first step is to determine the prevalence of high risk HPV infections in such cases and control samples, *i.e.*, cervical biopsy tissues. Previous studies from our laboratory have identified that over 70% of cervical cancers are HPV16 positive, followed by HPV18 and some other types, with small proportion of 2%, lacking HPV infections.

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