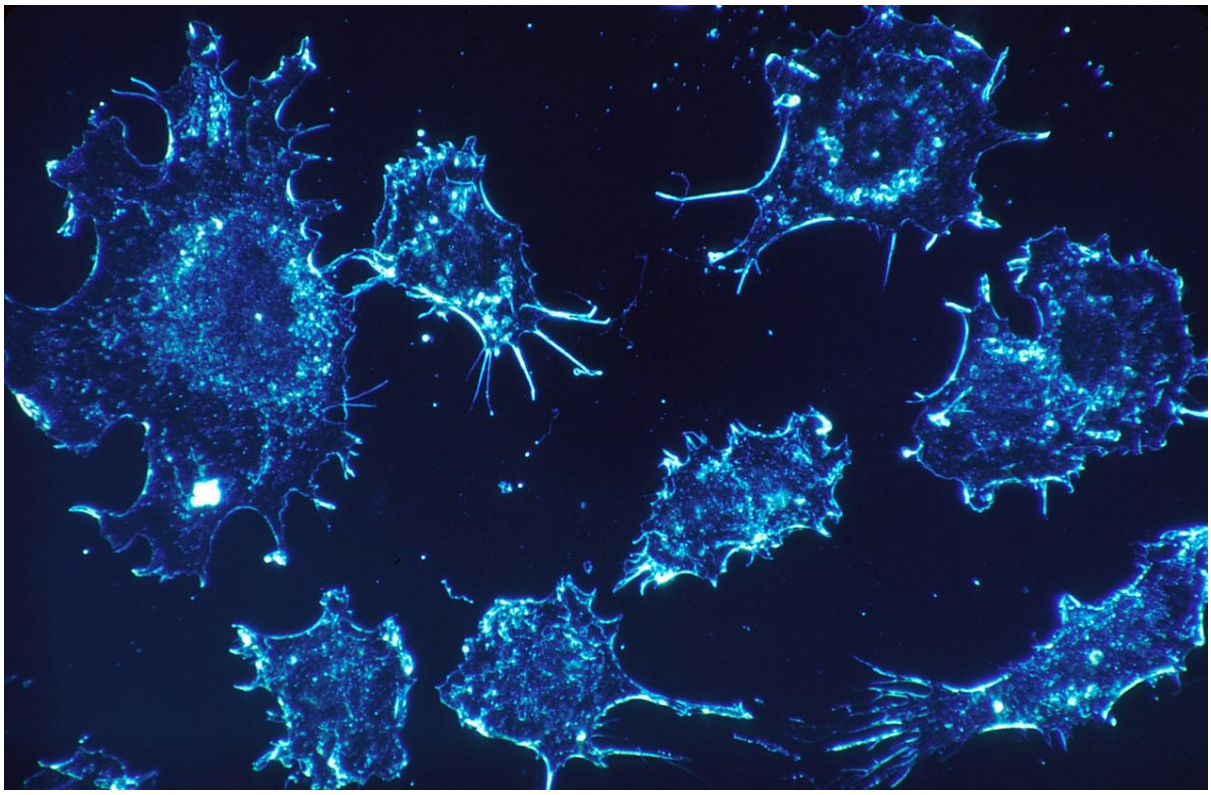
DBT-NIBMG scientists working to understand cervical cancer better

New Delhi, Dec 03: Cervical cancer is the second most frequent cause of cancer-related deaths among Indian women. A major risk factor, which accounts for 99.7% cases of cervical cancer is persistent infection with Human Papilloma Virus (HPV). HPV16 accounts for greater than 70% of the cervical cancer cases in most countries.



E6 and E7 are two oncoproteins encoded by HPV16. It has been found that E6 and E7 deregulates and functionally inactivate p53 and pRb and promotes cervical cancer. In recent years, several publications have shown that the non-coding RNAs like miRNA and long noncoding RNA (lncRNA) play different roles in the normal cellular physiology and molecular pathogenesis of several diseases, including cancer. The altered expression of miRNA and lncRNA in many cancer types has been explored as a marker for possible diagnosis and therapy.

Recently, a new regulatory circuit has been identified in which lncRNA mediates the post transcriptional control of microRNAs at the level of Drosha processing. LncRNAs are non-protein coding RNA molecules larger than 200 nucleotides, functionally similar to mRNAs in being transcribed by RNA polymerase II, being polyadenylated and being spliced.

LncRNAs have a huge role in different biological processes such as dosage compensation, imprinting, homeotic gene expression, proliferation, differentiation, cell cycle progression and apoptosis. Several lncRNAs, including HOX Transcript Antisense RNA (HOTAIR),

have been found to act as key regulators of cancer development through reprogramming the cellular chromatin state.

Previous studies at National Institute of Biomedical Genomics (DBT-NIBMG) have unveiled a mechanism of HPV16 E7-mediated increase of gene expression globally, by impairing lncRNA HOTAIR expression and function. Further they also highlighted the ability of E7 to increase HOX gene expression by epigenetic regulation and their association with EMT in HPV16 positive cervical cancer. Interestingly, a genetic variation within HOTAIR gene, results in creation of miR-22 binding site in cervical cancers and upregulation of this miR-22 could lead to down- regulation of HOTAIR expression, in such cases. The latter study is indicative of a cross-talk between lncRNA and miRNA in cervical cancer pathogenesis.

Researchers at the Institute are exploring the involvement of miRNAs and long noncoding RNAs in HPV16 driven cervical cancers, the interaction of lncRNAs with cellular miRNAs, under the influence of E7 expression and to investigate how they influence HPV16 related CaCx pathogenesis employing a global assay approach. They are using both human tissue biopsy samples and cell line-based approaches to fulfill the goal.

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