DBT-NIBMG scientists explore cervical cancer pathogenesis

New Delhi, Nov 04: Cervical cancer or the cancer of the uteri cervix is the most frequent cause of cancer-related deaths among Indian women. It is caused by persistent infection with Human Papillomavirus (HPV). HPV infection is common among sexually active women but 70-90% of them clear off the infection within two years. Thus, infection with HPV is necessary but not sufficient for causing cervical cancer.

Among the different HPV types, HPV16 and HPV18 are the most prevalent, accounting for more than 70% of the cervical cancer cases. The virus works by interfering with host transcriptional machinery with its oncoproteins E6 and E7. It is well established that oncoproteins E6 and E7 interact with the tumor suppressor p53, and pRb respectively, thereby contributing to cellular transformation and neoplastic progression.

The viral oncoproteins are also known to interact with multitudes of other host encoded molecules and interfere with fundamental processes by modulating host transcriptional machinery, but the mechanisms of these interactions are still not understood completely.

The viral oncoprotein E7 interacts with pRb and E2F transcription factors, which in turn interacts with the Polycomb group of proteins to orchestrate and mediate global gene expression leading to gene silencing. Thus, E7 could probably act as a master regulator of gene expression alterations in cervical cancers.
The altered gene expression may also be correlated with the natural polymorphisms or genetic variations across the genomes between individuals. Although the current dogma is that HPV integrates into the host genome and thereby drives cervical carcinogenesis, it is also observed that a large proportion of such cancers harbor HPV genomes in the episomal forms, either pure or concomitant with integrated forms.

Studies conducted at DBT- National Institute of Biomedical Genomics (DBT-NIBMG) has shown that the two different categories of cervical cancer groups (episomal and integrated forms) are molecularly distinct, which calls for extensive characterization of the two subtypes of such cancers, by high throughput assays in order to get a holistic insight into the molecular mechanisms of transformation prevailing in these cancers and to identify suitable markers for risk prediction and prognosis. Such studies, which are underway, will enable us to draw insights into the disease pathogenesis and identification of specific targets for tackling such cancers.

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