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Modulation of FoxM1 SUMOylation by high-risk HPV and its significance in cervical cancer

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Cervical cancer is the leading cause of death in women worldwide and is primarily associated with persistent infection of high-risk human papillomavirus (HPV). The oncogenic transcription factor, Forkhead box M1b (FoxM1b) is often overexpressed in many human tumors including cervical cancer, signifying its participation in tumorigenesis. Its proven role in carcinogenesis and its prospect as a promising therapeutic in cancer makes it a molecule of considerable clinical interest. Interestingly, post-translational modifications of FoxM1 have been shown to modulate its activity in cell cycle control, genomic stability and tumorigenesis. A thorough understanding of FoxM1 will be extremely useful in the innovation of more rationalized strategies for treating and preventing cancer. Here, we report that FoxM1b interacts with SUMOylating enzymes Ubc9 and PIAS1 and subjected to SUMOylation. We also demonstrate that SUMOylation contributes to destabilization and nucleocytoplasmic shuttling of FoxM1b protein. More importantly, our work provides the first evidence regarding a role of E7 oncoprotein in HPV mediated upregulation of FoxM1b. The elevated expression of FoxM1 was determined to be posttranscriptional and was attributed to decreased SUMOylation of FoxM1b in the E7-expressing cells. Thus, our study provides valuable insights into SUMOylation dynamics of FoxM1bas well as identifies the biochemical mechanism that high risk HPV exploits to induce malignant transformation. Altogether, the investigation enriches our understanding of the mechanisms of HPV oncogenesis in development of cervical carcinoma which may facilitate in the discovery of new anticancer strategies.

Biography

Neha Jaiswal is currently persuing PhD from University of Delhi South Campus. Her research interest focuses on the elucidation of mechanisms underlying HPV mediated oncogenesis. She has authored four peer reviewed publications. She has also attended several national and international conferences and has several poster awards to her credit. Her work was also selected for oral presentation and received an award of excellence at 3rd International Conference of Carcinogenesis Foundation in 2012.

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