

## Abstract

Efficient understanding of carcinogenesis and its early detection requires multimodal studies and cervical cancer research is no exception. Besides cytopathology and molecular pathology, biophysical characterization of cells (viz. electrical, mechanobiological) are thus elucidatory. *In vitro* studies on normal keratinocytes and cervical cancer cells under assaults encompassing cyto-morphometric and biophysical attributes hence may be effective for value addition to cervical smear analysis. In assessing malignant potentiality of cervical lesions, tissues may be studied by both non-invasive optical coherence tomography and invasive histopathology and molecular pathology techniques to record changes in optical properties and transcriptomic as well as proteomic attributes respectively. In this study biophysical and immunocytochemical analysis of normal keratinocyte and cervical cancer cell (HeLa) *in vitro* under chemical assaults documented their behavioural discrepancy having relevance to improving cytopathological screening. Cellular biophysical attributes provided signatures well ahead of morphological changes. A low cost liquid-based cytological technique for cervical monolayer was developed to enhance sensitivity of cervical screening by manual and automated approaches and to classify normal and abnormal conditions as per cellular electrical impedance. Global gene expression micro-array analysis done by self-organizing map, depicted differences in cervical pre-cancer and cancer, in respect to involvement of chromosomes and gene clusters exhibiting unique and dominant features. Optical biopsy depicted differential optical intensity distribution in normal and diseased conditions whereas semi-quantitative immunohistochemical attributes illustrated up-regulation of epithelial master regulator (p63), cytokeratin5/6, cytoplasmic E-cadherin and  $\beta$ -catenin, Hif1 $\alpha$ , c-myc, CD105 in cervical pre-cancer and its malignant transformation which were logically corroborative with optical biopsy. Thus present study depicted (i) multi-modal feature differences in normal epithelial and cervical cancer cells under assaults, (ii) efficacy of newly developed low-cost liquid based cytology for cervical smear screening and in classifying its normal and abnormal conditions as per cellular electrical impedance, (iii) emerging trends of global gene expressions and (iv) corroborative optical biopsy features and immunohistochemical attributes for prime candidate genes in cervical pre-cancer and cancer which were effective in providing multimodal pathobiological insight for cervical carcinogenesis and also in augmenting cancer screening.

**Keywords:** Cervical Cancer, Multi-modal Analysis, Cellular Electrical Impedance, Molecular Pathology, Global Gene Expression, Immunohistochemistry, Semi-quantitative Analysis