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Invasive Cervical Carcinoma Genetic Heterogeneity: Biological and Clinical Significance

Human chromosomal abnormalities are a hallmark of cancer and include both numerical and structural aberrations. High-risk human papillomaviruses (HPV) are associated with nearly all invasive cervical carcinomas (ICC); worldwide, ICC is the second most common female cancer. The two HPV-encoded oncoproteins, E6 and E7, have been implicated in mitotic infidelity by their ability to induce centrosome-related mitotic disturbances. The aim of this study is to investigate the heterogeneity, interrelationship and clinical significance of numerical chromosome abnormalities, HPV DNA viral load (measured by QPCR), chromogenic *in situ* hybridization (CISH) signal patterns for HPV DNA, HPV E6 and E7 mRNA and microRNAs (miR-7, miR-21, miR-34a, miR-143, miR-210) and immunohistochemical markers of DNA damage repair (DDR) pathways in 100 HPV16 positive ICC. Currently, CISH for centromere 7 has been performed on 81 formalin-fixed, paraffin-embedded (FFPE) ICC and compared with histopathological grade, HPV DNA CISH and viral load. Chromosome 7 monosomy and polysomy show statistically significant differences when compared with well and moderate ($P=0.020$), and well and poorly differentiated ICC ($P=0.025$). Trisomy and tetrasomy were significantly more common in well, than in moderately and/or poorly differentiated ICC ($P<0.05$); pentasomy was significantly more common in poorly than in well or moderately differentiated ICC ($P<0.01$). Changes to numerical chromosome number did not correlate with HPV DNA viral load ($P>0.05$). Our preliminary data indicate the importance of aneusomies in the development and progression of ICC from well to poorly differentiated tumor grade. Polysomy may represent a useful biomarker of ICC aggressiveness.