P10.06 PROGNOSTIC IMPORTANCE OF DNA REPAIR GENE POLYMORPHISMS IN CERVICAL CANCER PATIENTS FROM INDIA

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Background The cell's ability to repair DNA damage is important. Genetic variation in DNA repair genes can modulate DNA repair capacity and may be related to cancer risk. Human papillomavirus (HPV) is considered to be a necessary but not sufficient cause for cervical cancer and, therefore, other factors contribute to the carcinogenic process.
Objectives To evaluate polymorphisms in the DNA repair genes: XRCC1 (Arg194Trp, Arg280His, and Arg399Gln), ERCC1 (Asp118Asp), ERCC2 (Lys751Gln) and ERCC4 (Arg415Gln) with the risk of cervical cancer progression and to analyse their expression profile.
Material and methods A case control study consisting of 178 samples [65 cervical cancer (CaCx), 45 squamous intraepithelial lesion (SIL) and 68 controls] was carried out. Genotypes were determined by PCR-RFLP and DNA sequencing. Expression analysis was done by RT-PCR and Western blotting.
Results Positive association was seen between the polymorphisms of XRCC1 genes i.e., in codons 194 (OR = 20.1, 95% CI = 5.9–68.8), 280 (OR = 5.4, 95% CI = 2.3–12.6) and 399 (OR = 4.2, 95% CI = 1.5–12.1) and cervical cancer. SIL patients also showed a significant association with codon 194 (OR = 7.56, 95% CI = 3.42–16.70). Positive correlation was also found in ERCC4 Gln415Gln in both CaCx and SILs (OR = 21.3 95% CI = 7.1–64.0 and OR = 7.8, 95% CI = 2.9–20.9, respectively). For ERCC2 Gln751Gln the association was significant for both CaCx (OR = 10.1, 95% CI = 2.6–37.9) and SILs (OR = 8.9, 95% CI = 2.8–28.3). However the risk for CaCx and SILs did not appear to differ significantly amongst individuals featuring the ERCC1 Asp118Asp genotype. The invasive cancer and SIL subjects also demonstrated lower relative expression of the above DNA repair genes at both mRNA and protein level ($p < 0.001$).
Conclusions This study indicates that variant types of DNA repair genes play an important role in modifying individual susceptibility to cervical cancer. Since cervical cancer is a multi-factorial disease, the contribution of DNA repair enzymes to the development of cervical cancer, if it exists may be concealed by HPV infection.
Disclosure of interests The authors declare that they have no competing interests.

P10.07 MAPPING THE INTEGRATION SITES E1-E2 OF HPV-16 ANDHPV-18 AS A TOOL TO EVALUATE DIFFERENT STAGES OF CERVICAL DISEASE PROGRESSION

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Introduction Different methodologies have been developed to analyse integration. Most of them are expensive and laborious. Since the most frequent disrupting happen in E1 or E2 genes we believe that amplify fragments covering theses genes could be associated to virus integration status.
Methods Hence, in order to evaluate the physical state (episomal or integrated) of HPV 16 and 18 genomes, a PCR combining 10 primers pairs for HPV16 and 11 primers pairs for HPV18 were used, covering the E1-E2 region, adapted as described by Vernon *et al*. (1997)[1] and Collins Constandinou-Williams *et al*. (2009).[2] CASKI and HeLa lineage were used as control.
Results Our preliminary results involved 93 samples cervical samples from patients infected by HPV16 and 37 by HPV18, harbouring cervical lesions in different stages of progression, except HPV18, exclusively associated with cancer lesions. Among HPV16, 26 (28%) were presented episomal, 30 (32%) mixed and 37 (40%) integrated forms. The upper region E1a were the most frequently absent (disrupted) (n = 30, 32%), followed by the downstream E2c region, (n = 21, 22,6%). Among HPV 18 cervical cancers, 5 (13,5%) were presented as episomal forms, 8 (21,5%) mixed and 24 (65%) were integrated. The downstream region E2P3 was the most frequently disrupted, (n = 30, 81%).
Conclusion It is interesting to observe that literature points out a predominance of disruption in E2 region but our results suggested a highly prevalent E1 inactivation. The approach here described is a very specific methodology that can successfully map the HPV 16 and 18 genome fragile areas. Data are being analysed in order to search for statistical correlation between integration and severity of the lesion but it has been observed that E1-E2 absences were suggestively frequent in HSIL and cancer. In a few cases, episomal forms were observed in cancer samples, suggesting additional biomarkers as responsible for carcinogenesis.
Disclosure of interest statement PCR, Genomic integration, episomal, HPV16.

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P10.08 PREVALENCE OF LOW- AND HIGH-GRADE CERVICAL INTRAEPITHELIAL LESIONS AMONG FEMALE PARTICIPANTS IN PRIVATE HEALTH PLANS IN THE UNITED STATES, 2007–2013: ECOLOGIC EVIDENCE OF POPULATION EFFECTIVENESS OF HUMAN PAPILLOMAVIRUS VACCINATION

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Introduction Human papillomavirus (HPV) vaccine, which provides protection against oncogenic HPV types 16 and 18, was licensed in the United States (US) in late 2006. HPV 16 and 18 are associated with approximately 25% of low-grade and 50% of high-grade cervical intraepithelial lesions worldwide. HPV vaccination is recommended for US girls aged 11–12 years, with catch-up vaccination through age 26; in 2013 coverage among girls aged 13–17 was 57% for 1 dose and 38% for 3 doses.
Methods Using health care claims data from 9.7 million privately insured females aged 10–39 years, we estimated the annual