

RISK EVALUATION OF CERVICAL CANCER BASED ON THE INTERACTION OF HPV INFECTION AND MTDNA VARIATIONS AMONG CHINESE WOMEN.

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HPV infection is the main risk factors of cervical cancer, while genetic variations in mitochondrial DNA have been demonstrated associating with human carcinogenesis. The aim of the study was to find out the association among HPV infection, cervical cancers and genetic variations of mtDNA D-loop and Cyt B gene, to evaluate the risk of cervical cancer for Chinese women. All of the individual samples about HPV infection were studied by GP PCR-SBT method. The sequences were aligned by the ClustalX and Bioedit software, using Revised Cambridge Reference Sequence (rCRS) as a reference (gi: 115315770). χ^2 test was used to examine difference in age of patients with cervical cancer and controls. The associations between genetic variations and risk of cervical cancer were estimated by calculating the odds ratio (OR) and the 95% confidence interval (95% CI) with conditional logistic regression model adjusting for age when appropriate, using SPSS13.0 software. It was found that D150T had significant association with HPV infection. Associations of D-Loop variations between HPV-positive cervical cancers and HPV-negative controls, HPV-positive controls and HPV-negative controls as well as HPV-positive and negative subjects were investigated. Significant differences were found for D150 locus (OR=6.035, 95%CI=4.725-7.709, $p=5.761428089439e-047$; OR=7.468, 95%CI= 5.410-10.310, $p=2.393520314525e-034$; OR=5.592, 95%CI=4.453-7.023, $p=1.253266444391e-049$, respectively). The single nucleotide polymorphism of D150 (C150T may remodel mtDNA replication), D152 (T152C) and dinucleotide repeat D514 variation in D-Loop region were found to be susceptible to cervical cancer (OR=2.966, 95 % CI=2.731-3.222, $p=0.000$; OR=1.375, 95 % CI=1.245-1.519, $p=0.000$; OR=1.34, 95 % CI=1.252-1.438, $p=0.000$, respectively). There was no significant difference between cervical cancers and controls for the haplotype of D150-D152-D514. It was found that the variation of a mononucleotide repeat (CCCCCCC...TCCCCC) between 303-315 nucleotides (D310) and T146C variation according to MITOMAP in the mitochondria databank could not be considered as a marker of malignancy. Besides, Synonymous variations of T14783C, G15043A, A15301G and A15326G were found in Cyt B gene and no significant difference of these variations was found between cervical cancer patients and controls. There was no significant difference in age between cervical cancer patients and controls ($p=0.211$). It is possible that there is an interaction of C150T transition with HPV infection to cause cervical cancer. Besides, C150T, T152C transitions and D514 dinucleotide repeat variation may be considered as a susceptible factor to evaluate the risk of cervical cancer in Chinese women. In addition, it was indicated that there was no relationship between Cyt B gene variation and cervical carcinogenesis. It was suggested that mitochondrial DNA variation might contribute to cervical cancer development.

Keywords:

cervical cancer; HPV; mitochondrial DNA; risk evaluation, susceptibility