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Genetic Polymorphisms of DNA Double Strand Break Gene *Ku70* and Gastric Cancer in TaiwanMeng-Hsuan Lee¹, Fang-Jing Li¹, Mei-Due Yang¹, Meng-Chun Lu¹, Hwei-Chung Wang¹, Wen-Shin Chang¹, Chia-Wen Tsai¹, Chih-Hsueh Lin¹, Cheng-Chieh Lin¹, Da-Tian Bau^{1#}¹Terry Fox Cancer Research Lab, China Medical University & Hospital

The DNA repair gene *Ku70*, an important member of non-homologous end-joining repair system, is thought to play an important role in the repairing of DNA double strand breaks. It is known that defects in double strand break repair capacity can lead to irreversible genomic instability. However, the polymorphic variants of *Ku70*, have never been reported about their association with gastric cancer susceptibility. In this hospital-based case-control study, the associations of *Ku70* promoter T-991C (rs5751129), promoter G-57C (rs2267437), promoter A-31G (rs132770), and intron 3 (rs132774) polymorphisms with gastric cancer risk in a Taiwanese population were investigated. In total, 136 patients with gastric cancer and 560 age- and gender-matched healthy controls recruited from the China Medical Hospital in Taiwan were genotyped. As for *Ku70* promoter T-991C, the ORs after adjusted by age and gender of the people carrying TC and CC genotypes were 2.41 (95% CI=1.53-3.88) and 3.21 (95% CI=0.96-9.41) respectively, compared to those carrying TT wild-type genotype. The *P* for trend was significant ($P < 0.0001$). In the dominant model (TC plus CC versus TT), the association between *Ku70* promoter T-991C polymorphism and the risk for gastric cancer was also significant (adjusted OR=2.48, 95% CI=1.74-3.92). When stratified by age and gender, the association was restricted to those at the age of 55 or elder of age (TC vs TT: adjusted OR=2.52, 95% CI=1.37-4.68, $P=0.0139$) and male (TC vs TT: adjusted OR=2.58, 95% CI=1.33-4.47, $P=0.0085$). As for the other three polymorphisms, there was no difference between both groups in the distributions of their genotype frequencies. In conclusion, the *Ku70* promoter T-991C (rs5751129), but not the *Ku70* promoter C-57G (rs2267437), promoter A-31G (rs132770) or intron 3 (rs132774), is associated with gastric cancer susceptibility. This polymorphism may be a novel useful marker for gastric carcinogenesis.

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Synergistic Cytotoxic Effects of Arsenic Trioxide plus Dithiothreitol on Mice Oral Cancer Cells

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The anti-tumor properties of arsenic trioxide have attracted extensively attention after its successful inducing apoptosis of acute promyelocytic leukemia cells. However, the therapeutic spectrum should not only be restricted to acute promyelocytic leukemia, but should also extend into other tumor cells. In this study, we aimed at investigating its potential application to clinical therapeutics in oral cancer. In this preclinical animal test, primarily cultured cells from the tumor sites and normal sites of a two-drug 200 µg/ml 4-nitroquinoline 1-oxide (4NQO) plus 500 µg/ml arecoline-induced oral cancer C57BL/6J Narl mice model were examined of their viabilities after the treatments of arsenic trioxide with/without other drugs. In this model, the mice were treated with 4NQO plus arecoline (NA) in their drinking water for eight weeks (8-w), and then removed the drugs for another 10 or 20 weeks (18-w and 28-w, respectively). The results showed that although 2 µM of arsenic trioxide 24-h treatment can suppress the viabilities of cells primarily cultured from the tumor sites of 8-w, 18-w and 28-w NA-treated mice to 72.9%, 71.5% and 65.6%. However, it can also suppress the viabilities of cells from the sham-treated mice of 8-w, 18-w and 28-w to 76.8%, 73.4% and 75.7%, respectively. The co-cytotoxicity of dithiothreitol and arsenic trioxide on primarily cultured cells from oral cancer mice should be confirmed in human oral cancer cell lines before its application in clinical therapy, and the detailed mechanism is worth further investigation.

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