# Polymorphisms in cell cycle regulatory genes;urinary arsenic profile and urothelial carcinoma

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摘要

**Abstract**

ntroduction: Polymorphisms in p53, p21 and CCND1 could regulate the progression of the cell cycle and might increase the susceptibility to inorganic arsenic-related cancer risk. The goal of our study was to evaluate the roles of cell cycle regulatory gene polymorphisms in the carcinogenesis of arsenic-related urothelial carcinoma (UC). Methods: A hospital-based case-controlled study was conducted to explore the relationships among the urinary arsenic profile, 8-hydroxydeoxyguanosine (8-OHdG) levels, p53 codon 72, p21 codon 31 and CCND1 G870A polymorphisms and UC risk. The urinary arsenic profile was determined using high-performance liquid chromatography (HPLC) and hydride generator-atomic absorption spectrometry (HG-AAS). 8-OHdG levels were measured by high-sensitivity enzyme-linked immunosorbent assay (ELISA) kits. Genotyping was conducted using polymerase chain reaction-restriction fragment length polymerase (PCR-RFLP). Results: Subjects carrying the p21 Arg/Arg genotype had an increased UC risk (age and gender adjusted OR=1.53; 95% CI, 1.02-2.29). However, there was no association of p53 or CCND1 polymorphisms with DC risk. Significant effects were observed in terms of a combination of the three gene polymorphisms and a cumulative exposure of cigarette smoking, along with the urinary arsenic profile on the UC risk. The higher total arsenic concentration, monomethylarsonic acid percentage (MMA%) and lower dimethylarsinic acid percentage (DMA%), possessed greater gene variant numbers, had a higher UC risk and revealed significant dose-response relationships. However, effects of urinary 8-OHdG levels combined with three gene polymorphisms did not seem to be important for UC risk. Conclusions: The results showed that the variant genotype of p21 might be a predictor of inorganic arsenic-related UC risk.