

## The Association between Gene Polymorphisms of GPX, SEPP1, and SEP15, Plasma Selenium Levels, Urinary Total Arsenic Concentrations, and Prostate Cancer

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**Abstract :** Prostate cancer occurs in men over the age of 50, and rank sixth of the top ten cancers in Taiwan, and the incidence increased gradually over the past decade in Taiwan. Arsenic is confirmed as a carcinogen by International Agency for Research on (IARC). Arsenic induces oxidative stress may be a risk factor for prostate cancer, but the mechanism is not clear. Selenium is an important antioxidant element. Whether the association between plasma selenium levels and risk of prostate cancer are modified by different genotype of selenoprotein is still unknown. Glutathione peroxidase, selenoprotein P (SEPP1) and 15 kDa selenoprotein (SEP 15) are selenoprotein and regulates selenium transport and the oxidation and reduction reaction. However, the association between gene polymorphisms of selenoprotein and prostate cancer is not yet clear. The aim of this study is to determine the relationship between plasma selenium, polymorphism of selenoprotein, urinary total arsenic concentration and prostate cancer. This study is a hospital-based case-control study. Three hundred twenty-two cases of prostate cancer and age ( $\pm 5$  years) 1:1 matched 322 control group were recruited from National Taiwan University Hospital, Taipei Medical University Hospital, and Wan Fang Hospital. Well-trained personnel carried out standardized personal interviews based on a structured questionnaire. Information collected included demographic and socioeconomic characteristics, lifestyle and disease history. Blood and urine samples were also collected at the same time. The Research Ethics Committee of National Taiwan University Hospital, Taipei, Taiwan, approved the study. All patients provided informed consent forms before sample and data collection. Buffy coat was to extract DNA, and the polymerase chain reaction - restriction fragment length polymorphism (PCR-RFLP) was used to measure the genotypes of SEPP1 rs3797310, SEP15 rs5859, GPX1 rs1050450, GPX2 rs4902346, GPX3 rs4958872, and GPX4 rs2075710. Plasma concentrations of selenium were determined by inductively coupled plasma mass spectrometry (ICP-MS). Urinary arsenic species concentrations were measured by high-performance liquid chromatography links hydride generator and atomic absorption spectrometer (HPLC-HG-AAS). Subject with high education level compared to those with low educational level had a lower prostate cancer odds ratio (OR). Mainland Chinese and aboriginal people had a lower OR of prostate cancer compared to Fukien Taiwanese. After adjustment for age, educational level, subjects with GPX1 rs1050450 CT and TT genotype compared to the CC genotype have lower, OR of prostate cancer, the OR and 95% confidence interval (CI) was 0.53 (0.31-0.90). SEPP1 rs3797310 CT+TT genotype compared to those with CC genotype had a marginally significantly lower OR of PC. The low levels of plasma selenium and the high urinary total arsenic concentrations had the high OR of prostate cancer in a significant dose-response manner, and SEPP1 rs3797310 genotype modified this joint association.

**Keywords :** prostate cancer, plasma selenium concentration, urinary total arsenic concentrations, glutathione peroxidase, selenoprotein P, selenoprotein 15, gene polymorphism

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