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Association of GPX1 polymorphism, GPX activity and prostate cancer risk

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Abstract
Prostate cancer is the second most common cancer in men worldwide. Although the aetiology of this disease remains largely unclear, several lines of evidence suggest that oxidative stress plays a role in prostate carcinogenesis. The antioxidant enzyme glutathione peroxidase 1 (GPX1) is part of the enzymatic antioxidant defence, preventing oxidative damage to DNA, proteins and lipids by detoxifying hydrogen and lipid peroxides that may contribute to prostate cancer development. Some studies indicate an association between GPX1 Pro198Leu polymorphism and an increased risk of cancer. The purpose of the present study was to determine the possible association of GPX1 Pro198Leu polymorphism and erythrocyte GPX activity with the risk of developing prostate cancer and to clarify whether erythrocyte GPX activity levels were correlated with the GPX1 Pro198Leu genotype in the Turkish population. The GPX1 Pro198Leu genotype was determined in 33 prostate cancer patients and 91 control individuals. As evident from our results, there was no difference between genotype and/or allele frequencies in prostate cancer patients and controls. No significant difference was found in GPX1 genotype or allele frequency between aggressive and non-aggressive prostate cancer patients. It can be suggested with these findings that individual susceptibility of prostate cancer may be modulated by GPX1 polymorphism, but it needs further studies.

Keywords
prostate cancer; glutathione peroxidase 1; genetic polymorphism; oxidative stress

Introduction
Prostate cancer continues to be a major age-related malignancy with most incidences occurring between 54 and 75 years and rapid onset after 45 years. Evidence from epidemiological, experimental and clinical studies suggests that prostate cancer cells are exposed to an increased oxidative stress.¹,² Reactive oxygen species (ROS), most notably the hydroxyl radicals, generated endogenously by cellular metabolism are known to cause oxidative DNA damage that has been implicated in prostate carcinogenesis.³

The antioxidant enzyme glutathione peroxidase 1 (GPX1) is part of the enzymatic antioxidant defence, preventing oxidative damage to DNA, proteins and lipids by detoxifying hydrogen and lipid peroxides.⁴,⁵ The cytosolic form of GPX1 belongs to a family of selenium-dependent peroxidases that include cytosolic GPX,⁶ plasma-based GPX3⁷ and phospholipid hydroperoxidase GPX4.⁸ GPX1 knockout mice have a normal phenotype but are highly sensitive to oxidative stressors.⁹ Human GPX1 gene was found to possess several polymorphisms. The GPX1 gene has a GCG repeat polymorphism in exon 1, coding for a polyalanine tract of five to seven alanine residues.