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Manganese superoxide dismutase (*MnSOD*) genetic polymorphism is associated with risk of early-onset prostate cancer

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Prostate cancer continues to be the most frequently diagnosed neoplasm, and the second leading cause of cancer-related mortality in men. Oxidative stress may enhance prostatic carcinogenesis. Manganese superoxide dismutase (MnSOD) is the only known superoxide scavenger in mitochondria. It plays a key role in antioxidant defense as mitochondria are important for oxidative metabolism coupled to the electron transport chain and oxidative phosphorylation and hence, ROS production. A T→C single nucleotide substitution, resulting in a Val→Ala change at position 9 (Ala-9Val), which alters the secondary structure of the protein, has been noted to affect transport of MnSOD into the mitochondria. We have determined the MnSOD genotype in 85 prostate cancer cases and 151 control subjects. Ala-9Val polymorphism was determined using real time polymerase chain reaction (PCR) amplification with fluorescently labeled primers. No significant difference was found in prostate cancer susceptibility in the subjects with Ala/Ala and Val/Ala genotype compared with Val/Val genotype (Odds ratio (OR), 1.3; 95% confidence interval (95% CI), 0.69–2.42; $p = 0.416$). We did not observe an association of the MnSOD genotype or allele frequency between subgroups of cases divided by disease status (aggressive vs. non-aggressive prostate cancer). However, in the analyses stratified by the age at diagnosis we have observed that men homozygous for Ala had a 5.2-fold increased risk of early-onset prostate cancer (under age of 65) compared to men homozygous for Val allele ($p = 0.05$). These data suggest that Ala/Ala MnSOD genotype in the Macedonian population could have an influence on early onset of prostate cancer, but no impact on the subsequent development of the disease. Copyright © 2008 John Wiley & Sons, Ltd.

KEY WORDS — antioxidant enzymes; MnSOD genetic polymorphism; Macedonian population; oxidative stress; prostate cancer

INTRODUCTION

Prostate cancer continues to be the most frequently diagnosed neoplasm and the second leading cause of cancer-related mortality in men.[1] Oxidative stress, along with the formation of reactive oxygen species (ROS), is likely to play a role in the etiology of prostate cancer.[2] ROS are generated by normal metabolic processes *in vivo* and can initiate a cascade

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