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Letter to the Editor

Association between Genetic Polymorphisms of *SOD2* G1677T and 50 bp I/D of *SOD1* with the Risk of Colorectal Cancer

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Dear Editor-in-Chief

According to WHO, colorectal cancer (CRC) is a major cause of death in the world (1). An imbalance between oxidants and antioxidants causes oxidative stress that plays an important role in cancer (2). There are a lot of defense mechanisms to inhibit the toxic effects of reactive oxygen species, such as superoxide dismutase (3). Therefore, we investigated the possible association between genetic polymorphisms of superoxide dismutase 1 (*50bp I/D*) and superoxide dismutase *2* (*G1677T*) genes with development of colorectal cancer.

This case-control study included 214 colorectal cancer patients (79 females, 135 males) with a mean age of 54.5±14.1 and 237 (71 females, 166 males), healthy individuals as a control group mostly matched by gender and age with a mean age of 53.3±10.8. The present study was performed in Shiraz (Fars Province, southern Iran) in 2015.

Our study was approved by the Ethics Committee of the Shiraz University and was conducted with prior knowledge of the participants which included a written consent.

Genotyping of *SOD1* 50bp I/D (OMIM number 147450) was done by PCR and *SOD2* G1677T (OMIM number 147460) was done by polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP) method (4, 5). A Chi-Square test was performed for the *SOD2* G1677T and *SOD1* I/D polymorphisms to determine if the control group demonstrated hardy-Weinberg equilibrium.

The association between the genotypes of the study polymorphisms and colorectal cancer risk was assessed by calculating odds ratio (ORS) and 95% confidence intervals (CIs). A probability of $P<0.05$ was considered as statistically significant. The genotypic distribution of *SOD1* 50bp I/D and *SOD2* G1677T polymorphisms in the colorectal cancer patients and the controls are shown in Table 1. The *SOD1* and *SOD2* genotypes in the control subjects followed the Hardy-Weinberg equilibrium (for *SOD1* I/D polymorphism $\chi^2=1.061$, df=1, $P=0.05$) for *SOD2* G1677T polymorphism ($\chi^2=0.166$, df=1, $P=0.05$). Logistic regression analysis showed no significant association between *SOD1* 50bp I/D polymorphism (ID vs II: OR=0.89, 95%CI: 0.56-1.41, $P=0.626$; DD vs II OR=0.17, 95%CI: 0.02-1.48, $P=0.11$) and susceptibility to colorectal cancer and also no significant association was observed between the G1677T *SOD2* polymorphism and susceptibility to colorectal cancer. Neither the GT (OR=1.09, 95%CI: 0.72-1.64, $P=0.675$) nor the GG (OR=1.22, 95%CI: 0.70-2.15, $P=0.472$) genotypes altered the risk of colorectal cancer in comparison with the TT genotype. We also investigated the coincidence effect of *SOD1* 50bp I/D and *SOD2*

G1677T polymorphism and susceptibility to colorectal cancer (data not shown). Analysis showed no significant relationship between genotypes and risk of colorectal cancer.

Table 1: Association between genetic polymorphisms of *SOD1* 50bp I/D and *SOD2* G1677T and risk of colorectal cancer

Polymorphisms	*Controls*	*Cases*	*OR*	*95%CI*	*P*
SOD1 50bp I/D					
II	180	170	1.00	-	-
ID	51	43	0.89	0.56-1.41	0.626
DD	6	1	0.17	0.02-1.48	0.110
ID+DD vs II	57	44	0.81	0.52-1.27	0.375
Allele					
I	411	383	1.00	-	-
D	63	45	0.76	0.51-1.15	0.200
SOD2 G1677T					
TT	86	72	1.00	-	-
GT	116	106	1.09	0.72-1.64	0.675
GG	35	36	1.22	0.70-2.15	0.472
GT+GG vs TT	151	142	1.13	0.77-1.69	0.514
Allele					
T	288	250	1.00	-	-
G	186	178	1.10	0.845-1.439	0.473

Superoxide dismutase 1 and 2 genes products play a very important role in the defense against reactive oxygen species. Defects and some genetic polymorphism in either of these genes can affect their detoxification capacity and lead to cancer (6, 7). The present study is first report of the 50bp I/D polymorphism in the promoter region of *SOD1* and susceptibility to CRC. No significant association was observed between this polymorphism and risk of colorectal cancer.

Alterations in the 3' UTR of genes could led to increased stability leading to overexpression of proteins and thereby being responsible for pathogenesis of various disorders like cancer (8). *SOD2* G1677T is located in 3' UTR, we imagine the G1677T variant may cause colorectal cancer by regulating the expression of *SOD2* gene. Therefore the relationship of *SOD2* G1677T, one of the detoxification of ROS, with colorectal cancer was investigated. This was the first study about this subject in the world too. The results showed no significant relationship between this polymorphism and colorectal cancer.

Because of small sample size and limited risk factors investigated in the present study, and several genetic and environment factors usually involved in carcinogenesis, our conclusion remains to be further confirmed by studies of larger sample sizes and more risk factors among different races and regions so as to determine whether the *SOD1* 50bp I/D and *SOD2* G1677T polymorphisms would be a susceptible biomarker for colorectal cancer, and to evaluate whether there are interactions between gene and environment.

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Conflict of interest

The authors declare that there is no conflict of interest.

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