

LETTER to the EDITOR

TNF Polymorphisms and Cancer

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Dear Editor

Several meta-analyses recently have evaluated the accurate associations between TNF-alpha-238, -308 polymorphisms and cancer, indicating that TNF-alpha-238 polymorphism was not associated with cancers; however, TNF-alpha-308 polymorphism was positively associated with hepatocellular carcinoma and gastric cancer; whereas it was negatively associated with breast cancer only in Caucasian populations (Gorouhi et al., 2008, Yang et al., 2011a, Yang et al., 2011b, Zhou et al., 2011). The findings were interesting and complicated. Several considerations should be further discussed regarding the findings.

First, TNF-alpha-238, -308 polymorphisms differing relationships with cancers might due to different functions of the variants. It is still unclear whether the two polymorphisms could lead to different TNF-alpha production in human subjects, although in vitro studies reported that they could regulate the TNF-alpha expression (Zhou et al., 2011). It is interesting to design a population study to determine TNF-alpha in health human subjects and cancer patients with various genotypes of these polymorphisms, which would give readers more information of SNP functions on cancer development.

Second, TNF-alpha polymorphisms might also interact with other genetic factors in cancer development. Early studies have reported strong linkage disequilibriums between and HLA DR3, HLA-DRB1*0301 alleles and TNF-alpha-308 polymorphism (Javor et al., 2010, Feng et al., 2009). However, it is unknown with TNF-alpha-238 polymorphism and other genes. As TNF-alpha polymorphism is just a participant in the genetic pathopoiesis of cancers, large range of loci should be investigated regarding the interactions between them in the future study.

Third, TNF-alpha-308 polymorphism was only positively associated with hepatocellular carcinoma in Asians, and only negatively associated with breast cancer in Caucasian, suggesting that the polymorphism play different roles in different cancers because of ethnic specificities. However, the mechanisms are still unknown. To make the true relationships and mechanisms clear would be benefit for both Caucasian and Asian people cancer prevention and early diagnosis.

Fourth, now that TNF-alpha-308 is associated with breast, gastric cancer and hepatocellular carcinoma, moreover, the associations between it and other cancers should also be considered of interest and investigated in greater detail.

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Ren-Nan Feng^{1&}, Gui-You Liu^{2&}, Cheng Wang^{3&}, Chang-Hao Sun^{1*}, Ying Li^{1*}

¹Department of Nutrition and Food Hygiene, School of Public Health, ³Endemic Disease Control Center, Chinese Center for Disease Control and Prevention, Harbin Medical University, Harbin, ²Genome Analysis Laboratory, Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences, Tianjin, China [&]Equal contributors ^{*}For correspondence: changhao2002sun@gmail.com