



The TNF- α 238A polymorphism is associated with susceptibility to persistent bone marrow dysplasia following chronic exposure to benzene

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Abstract

Chronic exposure to benzene can result in transient hematotoxicity (benzene poisoning, BP) or persistent bone marrow pathology including dysplasia and/or acute myeloid leukemia. We recently described a persistent bone marrow dysplasia with unique dysplastic and inflammatory features developing in individuals previously exposed to benzene (BID) [Irons RD, Lv L, Gross SA, Ye X, Bao L, Wang XQ, et al. Chronic exposure to benzene results in a unique form of dysplasia. *Leuk Res* 2005;29:1371–80]. In this study we investigated the association of single nucleotide polymorphisms (SNP) (–863 (C → A), –857 (C → T), –308 (G → A), –238 (G → A)) in the promoter region of the cytokine, tumor necrosis factor- α (TNF- α) on the development of BP, persistent BID and *de novo* myelodysplastic syndrome (MDS) in 394 individuals. Only the –238 (G → A) polymorphism was significantly associated with the development of BID (odds ratio (OR) = 7.4; 95% C.I. 1.23–44.7) and was specific for BID and not *de novo* MDS or BP. These findings are consistent with a role for inflammation in the development of BID and suggest that cell-specific alterations in TNF- α expression may promote clonal selection in the evolution of neoplastic hematopoietic disease.

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1. Introduction

Benzene is a widely known hematotoxic agent. However, the severity of hematotoxicity associated with chronic exposure to benzene varies widely. Individuals undergoing comparable exposure may demonstrate no significant hematologic abnormalities while others exhibit signs of benzene poisoning (BP) or even bone marrow failure. Some individ-

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