Association between polymorphisms in \textit{ADAM33}, \textit{CD14}, and \textit{TLR4} with asthma in the Uygur population in China

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\textbf{ABSTRACT.} We evaluated the associations between single nucleotide polymorphisms (SNPs) and haplotypes of the genes encoding a disintegrin and metalloproteinase 33 (\textit{ADAM33}), cluster of differentiation 14 (\textit{CD14}), and Toll-like receptor 4 (\textit{TLR4}) and the susceptibility of developing specific adult phenotypes of bronchial asthma in a Chinese Uygur population. Five SNPs of \textit{ADAM33} (T1, T2, and V4), 3 SNPs of \textit{CD14} (-1359G/T, -1145G/A, and -159T/C), and 2 SNPs of \textit{TLR4} (-896A/G and -1196C/T) were genotyped in a Chinese Uygur sample of 126 adult asthmatic patients and
126 control subjects. Gene polymorphisms were detected by polymerase chain reaction-restriction fragment length polymorphism analysis. The genotyping results were confirmed in a random subgroup of our samples using direct DNA sequencing. The allele frequencies of ADAM33 T1 (TC), T2 (AG), and V4 (GG) were significantly higher in patients than in controls (P < 0.05). The genotypes T1 (TC+CC), T2 (AG+AA), and V4 (CG+GG) significantly increased the risk of asthma. After adjusting for confounding factors, these associations were stronger and remained significant. The T1 (TC) and V4 (GG) genotypes in the ADAM33 gene were associated with significantly decreased FEV1 levels in patients with asthma. The haplotype frequencies of Hap3 (CAC) and Hap4 (CAG) were significantly higher in patients than in controls (P < 0.05). Our results suggest that polymorphisms T1, T2, and V4 in ADAM33 may contribute to the susceptibility to asthma. Specific haplotypes of ADAM33 may contribute to a higher susceptibility to asthma in the Chinese Uygur population.

**Key words:** ADAM33, CD14, TLR4, Asthma, Polymorphisms, Uygur population