Matrix metalloproteinase gene polymorphisms and susceptibility to systemic sclerosis

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Genet. Mol. Res. 15 (4): gmr15049077
Received August 12, 2016
Accepted November 3, 2016
Published December 19, 2016
DOI http://dx.doi.org/10.4238/gmr15049077

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ABSTRACT. The major pathological hallmark of the systemic sclerosis (SSc) is skin and internal organ fibrosis, which results from normal tissue architecture alterations and extracellular matrix (ECM) protein deposition. ECM components are degraded by matrix metalloproteinases (MMP). Promoter region polymorphisms in MMP genes may influence gene expression, resulting in an imbalance between ECM protein production and degradation. Here, we analyzed *MMP1 -1607 1G/2G* (rs1799750), *MMP3 -1171 5A/6A* (rs3025058), and *MMP9 -1562 C/T*

(rs3918242) polymorphisms in relation to susceptibility to SSc and its clinical features. The patient group included 98 individuals with longstanding or recently diagnosed disease, meeting the American College of Rheumatology or LeRoy and Medsger criteria for SSc; the control group included 100 healthy blood donors. All participants were of European descent. Genotyping was performed by polymerase chain reaction followed by restriction digestion. Genotype and allele frequencies of MMP polymorphisms were similar between the two groups. In secondary analyses, significantly higher frequency of 1G/2G genotype from *MMP1* polymorphism was observed for patients testing positive for antinuclear autoantibodies (P = 0.007), while 1G/1G genotype was associated with interstitial lung disease development (P = 0.018). The 6A/6A genotype from *MMP3* polymorphism was absent in patients with calcinosis (P = 0.011), while the *MMP3* 5A/5A genotype correlated with the presence of anti-topoisomerase I antibodies (P = 0.009) and reduced diffusing capacity for carbon monoxide (P = 0.024). These results suggest that MMP polymorphisms are not associated with SSc susceptibility, although *MMP1* and *MMP3* variants are associated with specific SSc clinical and laboratory features.

Key words: Systemic sclerosis; Matrix metalloproteinase; MMP1; MMP3; MMP9; Genetic polymorphisms