

PADI4 Polymorphisms in Rheumatoid Arthritis

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Objectives : Peptidylarginine deiminase type 4 (PADI4) is an enzyme that catalyses the post-translational modification of peptidylarginine to citrulline, a reaction known as citrullination. Citrullination by PADI4 helps rheumatoid arthritis (RA)-specific autoantibodies recognize self-antigens. The purpose of this study is to investigate whether polymorphisms of PADI4 gene are associated with the susceptibility to RA in Korean population. **Methods** : Seven hundred and four patients with RA and 298 healthy unrelated controls were included in this study. The nucleotide sequences of PADI4 gene polymorphisms, which were in the promoter region at the -1445 A/G and in the exon 4 at the 27971 T/C, were analyzed by fluorescence resonance energy transfer (FRET) method. Association between RA and individual polymorphism was examined by Chi-square test. Haplotypes were reconstructed by using the Bayesian algorithm. **Results** : The genotype frequencies of the polymorphisms were in Hardy-Weinberg equilibrium. The distribution of genotypes and alleles did not differ between RA patients and controls. The four haplotypes were reconstructed based on the linkage disequilibrium at positions -1445 and 27971, but the distribution of haplotypes did not differ between two groups. Clinical features such as onset of age, sharp score/year and presence of rheumatoid factor and anti-cyclic citrullinated peptide antibody did not differ between both groups. The frequency of T allele at the position 27971 C/T polymorphism was higher among the RA patients than the control group, although there was no statistical significance ($p=0.058$). **Conclusion** : This study demonstrated that polymorphisms of the PADI4 gene may not contribute to disease susceptibility to RA in Korean population.

PADI4 polymorphisms and rheumatoid arthritis susceptibility: A meta-analysis.

고려대 류마티스내과

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We conducted a comprehensive meta-analysis with all available data on the association of allele (allele 2 vs 1) and genotype (2/2 vs 1/1, 2/2 vs 1/2, and 1/2 vs 1/1) of the whether peptidylarginine deiminase 4 (PADI4) polymorphisms with RA overall and in each ethnic population to explore whether PADI4 polymorphisms confer susceptibility to RA. Nine comparisons, 3 Asian and 6 European, from 8 studies were included in this meta-analysis. Overall meta-analysis shows a significant association of PADI4_94, 104 and 90 with RA (OR = 1.20, 1.17, 1.35, $p = 0.001$, < 0.0001 , 0.006, respectively). There was a significant association with all of the PADI4 polymorphisms with RA in people of Asian descent. However, there was no significant association of PADI4 polymorphisms with RA in people of European descent, except for PADI4_94. The presence of 2/2 genotype of the PADI4_94 significantly increased the risk for RA in European populations (OR = 2.10, 95% CI, 1.66 - 2.66, $p < 0.0001$) without between-study heterogeneity ($I^2 = 44.3$, $p = 0.15$). This meta-analysis demonstrates that the PADI4_94 polymorphisms may represent a significant risk factor for RA in Asians and Europeans and play a larger role in susceptibility to RA in Asian than in European populations.