

A Single-nucleotide Polymorphism of CCR6 (rs3093024) Is Associated with Susceptibility to Rheumatoid Arthritis But Not Ankylosing Spondylitis, in a Taiwanese Population

To the Editor:

Rheumatoid arthritis (RA) is a common autoimmune disease with chronic inflammatory reactions in the synovial tissue and joint destruction. Genetic and environmental factors contribute to the development of RA¹. Using genome-wide association analysis, Kochi, *et al* identified a single nucleotide polymorphism (rs3093024) in the *CCR6* gene that was associated with the risk of rheumatoid arthritis². Further, the genotype of *CCR6* correlated with the concentration of interleukin 17 in the sera of subjects with RA².

We investigated whether the polymorphism of *CCR6* is associated with susceptibility to RA in a Taiwanese population. A total of 1441 subjects were recruited [400 patients with RA, 361 with ankylosing spondylitis (AS), and 680 healthy subjects]. The patients with RA and the healthy subjects were from the Kaohsiung Medical University Hospital. The diagnosis of RA was according to the American College of Rheumatology 1987 revised criteria for the classification of RA. The 361 patients with AS were recruited from Chung Shan Medical University Hospital. Patients with AS who met the New York AS diagnosis criteria were asked to participate. Our study was approved by the institutional review boards of the hospitals. Informed consent was obtained before any data were collected from the subjects. DNA purification from buffy coat was done using the Genra Puregene Blood Kit (Qiagen, Valencia, CA, USA). Genotyping was performed using TaqMan allelic discrimination assays (Applied Biosystems, Foster City, CA, USA).

We found that the distribution of genotype rs3093024 was in accord with Hardy-Weinberg equilibrium for both cases and controls. Importantly, a significant association between rs3093024 genotype and the patients with RA was observed (AA/AG vs GG; OR 1.48, 95% CI 1.13–1.94, $p = 0.0046$; Table 1). Because the sex distribution between RA and control groups was very different, we further divided the original study subjects by sex and tested the sex-specific genetic effects of rs3093024. A significant association between rs3093024 and the risk of RA still existed (Table 1). The minor A allele of rs3093024 was associated with susceptibility to RA in the Taiwanese female population (AA/AG vs GG; OR 1.63, 95% CI 1.17–2.28, $p = 0.0038$; Table 1).

AS is also an autoimmune disease affecting mainly joints in the spine and the sacroiliac joint³. Recently, several genetic polymorphisms have

been strongly implicated in its pathogenesis^{4,5,6,7}. However, our results indicated that rs3093024 was not associated with susceptibility to AS (data not shown). We acknowledge that the modest AS sample size in the study was underpowered to detect the genetic effect of *CCR6*. A larger sample size is needed to replicate these findings.

We found a significant association between the genotype of *CCR6* (rs3093024) and the susceptibility to RA in a Taiwanese population. In agreement with previous reports in the Japanese population, our results strongly support the importance of the *CCR6* genotype in the risk of RA.

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Table 1. Genotyping and allele frequency of *CCR6* single-nucleotide polymorphism in patients with rheumatoid arthritis and in controls. Significant values are shown in bold type.

| Genotype | Cases (%), n = 400 | Controls (%), n = 680 | Genotype, p | p and OR (95% CI) | | Allelic, p |
|----------|-----------------------|--------------------------|-----------------|---------------------|---------------------|---------------------|
| | | | | Dominant, p | Recessive, p | |
| AA | 83 (21.3) | 107 (16.1) | 0.0081** | 0.0046** | 0.0323* | 0.0020** |
| AG | 197 (50.5) | 315 (47.2) | | 1.48 (1.13–1.94) | 1.42 (1.03–1.95) | 1.32 (1.11–1.58) |
| GG | 110 (28.2) | 245 (36.7) | | | | |
| A | 363 (46.5) | 529 (39.7) | | | | |
| G | 417 (53.5) | 805 (60.3) | | | | |
| Female | | | | | | |
| AA | 68 (21.3) | 55 (16.5) | 0.0122* | 0.0038** | 0.1173 | 0.0051** |
| AG | 166 (52.0) | 154 (46.3) | | 1.63 (1.17–2.28) | 1.37 (0.92–2.03) | 1.37 (1.10–1.70) |
| GG | 85 (26.7) | 124 (37.2) | | | | |
| A | 302 (47.3) | 264 (39.6) | | | | |
| G | 336 (52.7) | 402 (60.4) | | | | |

* $0.01 \leq p < 0.05$. ** $p < 0.01$.

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