Conclusions: These data suggest that steroid hormone-related genes play a role in determining the response to anti-TNF drugs.

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THU0012  TARGETED RE-SEQUENCING OF 128 RHEUMATOID ARTHRITIS SUSCEPTIBILITY GENES UNCOVERS NOVEL RISK LOCI IN THE SINGAPORE CHINESE POPULATION

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Background: Rheumatoid arthritis (RA) is a fairly common inflammatory autoimmune disease with a prevalence of 1% to 1.5%. Patients experience chronic joint pain, swelling and overtime irreversible joint damage. Genetic variants that contribute to rheumatoid arthritis (RA) susceptibility have been reported in more than 120 genes, including the HLA, PTTP22, CTLM4, TNFAIP3, PAD4, FCRL3, CD4, CD244 and CD40. The genetic susceptibility to RA has not been studied in the Singapore Chinese population.

Objectives: To identify novel risk variants in candidate genes previously reported to be associated with rheumatoid arthritis (RA) in Singapore Chinese RA patients positive for anti-citrullinated peptide antibodies (ACPA).

Methods: All the 128 known candidate genes associated with RA identified through GWAS were sequenced in 48 RA patients and 45 controls. The resultant data was analysed for association using single variant association and pathway-based association enrichment tests. In addition, the genetic burden due to rare variants was assessed using the C-alpha test. The candidate variants that showed significant association were validated in a larger cohort of 500 RA cases and 500 controls using mass array and Taqman technologies.

Results: 39 variants in 18 genes were identified using single variant association analysis and C-alpha test. IL6ST, with stepwise filtering. Among these, the mis-sense variant in IL6ST, 5:55260065 (p.Cys417Tyr) was significantly associated with RA in the Singapore Chinese patients (p=0.0194). The insignificant results of additional potential rare variants such as IL6ST, 5:55237103 and PXK rs199881366 is highly due to the limitations of our small sample size.

Conclusions: Our results suggest that IL6ST, 5:55260065, 5:55237103 and PXK rs199881366 confer risk of RA in ACPA-positive Chinese patients.

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