Association analysis in a Latin American population revealed ethnic differences in rheumatoid arthritis-associated SNPs in Caucasian and Asian populations

Castro-Santos P.

Verdugo R.A.

Alonso-Arias R.

Gutiérrez M.A.

Suazo J.

Aguillón J.C.

Olloquequi J.

Pinochet C.

Lucia A.

Quiñones L.A.

Díaz-Peña R.

Large genome-wide association studies (GWAS) have increased our knowledge of the genetic risk factors of rheumatoid arthritis (RA). However, little is known about genetic susceptibility in populations with a large admixture of Amerindian ancestry. The aim of the present study was to test the generalizability of previously reported RA loci in a Latin American (LA) population with admixed ancestry. We selected 128 single nucleotide polymorphisms (SNPs) in linkage equilibrium, with high association to RA in multiple populations of non-Amerindian origin. Genotyping of 118 SNPs was performed in 313 RA patients/487 healthy control subjects by mid-density arrays of polymerase chain reaction (PCR). Some of the identified associations were validated in an additional cohort (250 cases/290 controls). One marker, the SNP rs2451258, located upstream of T Cell Activation RhoGTPase Activating Protein (TAGAP) gene, showed significant association with RA ($p = 5 \times 10?3$), whereas 18 markers exhibited suggestive associations ($p < 0.05$). Haplotype testing showed association of some groups of adjacent SNPs around the signal transducer and activator of transcription 4 (STAT4) gene ($p = 9.82 \times 10?3$ to $2.04 \times 10?3$) with RA. Our major finding was little

replication of previously reported genetic associations with RA. These results suggest that performing GWAS and admixture mapping in LA populations has the potential to reveal novel loci associated with RA. This in turn might help to gain insight into the ?pathogenomics? of this disease and to explore trans-population differences for RA in general.