Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis with the prevalence rate of PsA in psoriasis...
patients estimated to be 14% in UK populations. PsA is a complex disease where disease liability is comprised of environmental risk factors and a polygenic susceptibility background. The genetics of PsA susceptibility is not fully understood; PsA is estimated to have a larger genetic component than psoriasis alone and recent studies have identified PsA-specific loci that begin to explain this increased burden, for example, amino acids in HLA-B and our own Immunochip study reported evidence for PsA-specific risk at chromosome 5q31 and IL23R.

Methods: In this study we attempt to validate 14 single nucleotide polymorphisms (SNPs) selected from our recent Immunochip study \((P < 1 \times 10^{-5})\) in a combined collection of 3139 PsA cases and 11 078 controls from UK, Republic of Ireland, Germany, Australia, Sweden and Italy. Genotyping was performed using the Life Technologies QuantStudio genotyping platform and association testing was performed using PLINK. For loci not previously reported for psoriasis we compare effect sizes using multinomial logistic regression, performed in Stata, and directly compare PsA genotypes from Immunochip \((n = 1936)\) to the psoriasis WTCCC2 study (excluding known PsA, \(n = 1784)\). To control for phenotype misclassification with RA, we include a genetic risk score comprised of the 41 RA susceptibility reported in the RA Immunochip study as a covariate and re-analysed the PsA Immunochip.

Results: We find genome-wide significant association to rs2476601, mapping to the gene PTPN22 \([P = 1.490 \times 10^{-9}, \text{OR} = 1.32]\). There was no evidence for association to rs2476601 in the psoriasis WTCCC2 cohort \((P = 0.34)\) and the effect estimates were found to be significantly different between PsA and psoriasis \((P = 3.2 \times 10^{-4})\). Direct comparison of genotypes for PsA and psoriasis found significant association to an increased risk of PsA \([P = 4.4 \times 10^{-4}, \text{OR} = 1.3]\). The association to PTPN22 in the PsA Immunochip data was not affected by the inclusion of the RA-GRS as a covariate. In addition, we find genome-wide significant association to the previously reported psoriasis risk loci; NOS2 \((rs4795067, P = 5.27 \times 10^{-9})\). No other SNPs reached genome-wide significance in the combined dataset.

Conclusion: For the first time, we report genome-wide significant association of PTPN22 \((rs2476601)\) to PsA susceptibility, a locus associated with many autoimmune diseases. The risk allele (A) and direction of effect are consistent with previous reports for RA and type I diabetes, but opposite of that reported for Crohn’s disease. We provide evidence that this is a PsA-specific risk locus as no association to psoriasis was observed in the WTCCC2 cohort and the effect estimates are significantly different between PsA psoriasis when compared in multinomial logistic regression.

Disclosure statement: The authors have declared no conflicts of interest.