

**PADI4 (rs2240340), PDCD1 (rs10204525), and CTLA4 (231775) gene
polymorphisms
and polyarticular juvenile idiopathic arthritis**

Abstract:

Background: Certain single nucleotide polymorphisms (SNPs) in genes such as PADI4 (coding for peptidyl arginine deiminase 4), PDCD1 (coding for programmed cell death 1), and CTLA4 (coding for cytotoxic T-lymphocyte-associated protein 4) are linked to rheumatoid arthritis (RA). However, links between SNPs rs2240340, rs10204525 and rs231775 in PADI4, PDCD1 and CTLA4 respectively, and juvenile idiopathic arthritis (JIA), the commonest type of childhood arthritis, are unclear.

We aimed to determine whether any of these SNPs are associated with JIA, and to clinical indices disease activity score (JADAS 71) and functional disability score (CHAQ).

Methods: We genotyped the three SNPs in 150 children with polyarticular JIA and 160 healthy children, recording standard health questionnaires, clinical features and laboratory markers.

Results: The TT genotype of PADI4 rs2240340 (aOR/95%CI 2.64: 1.31–5.30, $P = 0.006$) and CT genotype of PDCD1 rs10204525 (aOR/95%CI 4.99: 2.98–8.36, $P < 0.0001$) were associated with JIA. The AG+GG genotype of CTLA4 rs231775 was modestly linked to disease activity (aOR/95% CI 2.44 (1.19–5.04), $p = 0.015$). PADI4 rs2240340 was linked to CHAQ score (genotypes $p = 0.013$, alleles $p = 0.006$), whilst PDCD1 rs10204525 was linked to anti-CCP antibodies (genotypes $p = 0.004$), RF (genotypes $p = 0.01$), and the CHAQ score (genotypes $p = 0.005$, alleles $p = 0.013$).

Conclusions: There are various roles for these SNPs in PADI4, CTLA4 and PDCD1 in the diagnosis and, potentially, in the management of JIA.