on smoking status, PSC was associated with RA among never-smoking women (HR 1.42; 95% CI [1.07 to 1.88]), but not among ever-smoking women (HR 1.10; 95% CI [0.83;1.46]).

In the whole population, PSa was also positively associated with the risk of RA in all three models (HR 1.19; 95% CI [1.02 to 1.40] in Model 3). In stratified analyses on the smoking status, PSa was associated with an increased RA risk only among never-smoking women (HR 1.27; 95% CI [1.02 to 1.57]) and not among ever-smoking women (HR 1.18; 95% CI [0.93;1.44]).

**Conclusion:** In a large population-based prospective cohort study of French women, we reported that passive exposure to smoking during childhood or adulthood increased the risk of RA. The association was principally observed among never-smoking women. These results suggest that smoking by-products, whether actively or passively inhaled absorbed, could generate autoimmune, at least towards antigens involved in RA pathogenesis.

**REFERENCES:**


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**OP00014**

**HLA ASSOCIATIONS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS AND CLINICAL SUBTYPES**

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**Background:** Juvenile idiopathic arthritis (JIA) is a childhood onset rheumatic disease which is classified into seven different clinical subtypes based upon the ILAR classification criteria. The most common extra articular manifestation of JIA is its associated uveitis (JIAU); particularly chronic anterior uveitis (CAU). Uveitis is a serious complication with the potential to lead to ophthalmological damage and blindness. The rheumatoid factor negative polyarthritis and oligoarthritis ILAR subtypes, often referred to as the “poloyo” subgroup, are at a higher risk for developing JIAU, with up to 30% of polygos afflicted by CAU. The HLA region has long been reported as a genetic risk factor for JIA susceptibility, with evidence suggesting that different amino acids of HLA genes infer risk to different JIA subtypes.

**Objectives:** Investigate the association of amino acids and genetic variants in the HLA region with susceptibility to JIAU and the ILAR clinical subtypes.

**Methods:** Samples were genotyped using the Illumina Infinium CoreExome and Infinium Omniexpress arrays. Samples were excluded based on <98% call rate, discrepancy between genetically inferred sex and database records, inferred relatedness (identify-by-descent) and ancestral outliers based on principal component analysis (PCA). SNPs were excluded based on <0.01 minor allele frequency (MAF), and call rate <89%. SNP2HLA was used to impute HLA amino acids, SNPs and alleles. Analysis was then executed on markers with an information score >0.9 and MAF >0.1 using logistic regression or an omnibus test for multiallelic markers, including 3 PCs as covariates. Independent associations were identified using forward stepwise logistic regression including previously identified variants as covariates. Comparison of regression models was performed using a likelihood ratio test (LRT).

**Results:** We analysed 7425 markers within the HLA region in 450 JIAU and 2024 JIA cases without uveitis. The most significant association was to amino acid positions 13 of HLA-DRB1 (p=2.9×10⁻¹⁰⁰). Conditional analysis on DRB1 position 13 revealed an independent signal at DRB1 position 67 (p=2.4×10⁻⁴). Conditioning on all DRB1 alleles revealed an independent signal at HLA-DPB1 position 69 (p=5.3×10⁻¹⁰). As expected, ILAR subtype was found to be associated with JIAU (p=1.58×10⁻⁴). We used LRT to test if genetics provided further information above ILAR subtype alone and found that including residues at DRB1 position 13 significantly improved the fit of a model based on ILAR subtype alone (LRT p = 3.6×10⁻¹⁰⁰). The reciprocal analysis, adding ILAR subtype to a model based on DRB1 position 13 alone, did not significantly improve the fit of a model (LRT p = 0.83). Exploring associations in the polyglo subgroup (n=1646) we found significant associations to the three previously described amino acids and JIAU (DRB1 position 13 p=3.4×10⁻²⁰, DRB1 position 67 p=3.3×10⁻¹⁴, DBP1 position 69 p=2.2×10⁻¹⁰). Conclusion: This is largest analysis of HLA markers in JIAU patients to date since 2005. We identified two independent associations to lead to to visual impairment IA, and a further independent association to HLA-DPB1. This analysis demonstrates that including data on genetic risk factors adds further information to that captured...