

# Associations of human leukocyte antigen DRB with resistance or susceptibility to HIV-1 infection in the Pumwani Sex Worker Cohort

Lacap, PA; Huntington, JD; Luo, M; Nagelkerke, NJ; Bielawny, T; Kimani, J; Wachihi, C; Ngugi Elizabeth N.; Plummer, FA

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## Abstract:

**OBJECTIVE:** A group of commercial sex workers in the Pumwani Sex Worker Cohort, established in 1985 in Nairobi, Kenya, remain HIV-1 uninfected despite heavy exposure to HIV-1 through active sex work. Previous studies showed that this resistance is associated with a strong CD4+ T-cell response, which suggested that human leukocyte antigen class II antigens are important in resistance/susceptibility to HIV-1 infection. DRB1 is the most polymorphic locus among class II genes and forms haplotypes with DRB3, DRB4 and DRB5. The aim of this study is to investigate the role of DRB alleles/haplotypes on resistance/susceptibility to HIV-1 infection. **DESIGN:** In total, 1090 women enrolled in the Pumwani cohort were genotyped for DRB1, DRB3, DRB4 and DRB5 using a high-resolution sequence-based method. Allele/haplotype frequencies were compared between HIV-positive women and women who have remained HIV negative for more than 3 years despite frequent exposure. **METHODS:** Human leukocyte antigen DRB genes were amplified, sequenced and genotyped using a two-step sequence-based method. Allele/haplotype frequencies were determined using PyPop32-0.6.0. Statistical analysis was conducted using SPSS 11.0 for Windows. **RESULTS:** Three DRB1 alleles were associated with resistance: DRB1\*010101 (P = 0.016; odd ratio (OR): 2.55; 95% confidence interval (CI): 1.16-5.61), DRB1\*010201 (P = 0.019; OR: 1.86; 95% CI: 1.10-3.15), and DRB1\*1102 (P = 0.025; OR: 1.72; 95% CI: 1.07-2.78). DRB1\*030201 (P = 0.038; OR: 0.48; 95% CI: 0.23-0.98), DRB1\*070101 (P = 0.035; OR: 0.54; 95% CI: 0.30-0.97), DRB1\*1503 (P = 0.0004; OR: 0.34; 95% CI: 0.19-0.64), and DRB5\*010101 (P = 0.001; OR: 0.37; 95% CI: 0.20-0.67) were associated with susceptibility. The haplotype DRB1\*1102-DRB3\*020201 was associated with HIV-1 resistance (P = 0.041; OR: 1.68; 95% CI: 1.02-2.78), whereas the haplotypes DRB1\*070101-DRB4\*01010101 (P = 0.041; OR: 0.52; 95% CI: 0.28-0.98) and DRB1\*1503-DRB5\*01010101 (P = 0.0002; OR: 0.30; 95% CI: 0.15-0.58) were associated with susceptibility. These associations with resistance/susceptibility to HIV-1 were independent of previously reported alleles HLA-DRB1\*01 and HLA-A\*2301 **CONCLUSION:** Our findings indicate that human leukocyte antigen DRB-specific CD4+ T-cell responses are an important factor in resistance/susceptibility to HIV-1 infection