

Human leukocyte antigen-DQ alleles and haplotypes and their associations with resistance and susceptibility to HIV-1 infection

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Abstract:

Objectives: To determine the association of DQ antigens with resistance and susceptibility to HIV-1. **Design:** Despite repeated exposure to HIV-1, a subset of women in the Pumwani Sex Worker cohort established in Nairobi, Kenya in 1985 have remained HIV-1 negative for at least 3 years and are classified as resistant. Differential susceptibility to HIV-1 infection is associated with HIV-1 specific CD4⁺ and CD8⁺ T cell responses. As human leukocyte antigen-DQ antigens present viral peptides to CD4⁺ cells, we genotyped human leukocyte antigen -DQ alleles for 978 women enrolled in the cohort and performed cross-sectional and longitudinal analyses to identify associations of human leukocyte antigen -DQ with resistance/susceptibility to HIV-1. **Methods:** DQA1 and DQB1 were genotyped using taxonomy-based sequence analysis. SPSS 13.0 was used to determine associations of DQ alleles/haplotypes with HIV-1 resistance, susceptibility, and seroconversion rates. **Results:** Several DQB1 alleles and DQ haplotypes were associated with resistance to HIV-1 infection. These included DQB1 050301 (P=0.055, Odds Ratio=12.77, 95% Confidence Interval=1.44–112), DQB1 0603 and DQB1 0609 (P=0.037, Odds Ratio=3.25, 95% Confidence Interval=1.12–9.47), and DQA1 010201–DQB1 0603 0603 (P=0.044, Odds Ratio=17.33, 95% Confidence Interval=1.79–168). Conversely, DQB1 0602 (P=0.048, Odds Ratio=0.68, 95% Confidence Interval=0.44–1.05) and DQA1 010201–DQB1 0602 (P=0.039, Odds Ratio=0.64, 95% Confidence Interval=0.41–1.03) were overrepresented in the HIV-1 infected population. DQA1 0504-DQB1 0201, DQA1 010201–DQB1 0201, DQA1 0402-DQB1 0402 and DQA1 0402-DQB1 030101 genotypes were only found in HIV-1 positive subjects (Odds Ratio=0.30–0.31, 95% Confidence Interval=0.03–3.70), and these women seroconverted rapidly. The associations of these DQ alleles and haplotypes with resistance and susceptibility to HIV-1 were independent of the previously reported human leukocyte antigen-DRB 01, human leukocyte antigen A2/6802, and human leukocyte antigen-A 2301. **Conclusion:** The associations of DQ alleles and haplotypes with resistance and susceptibility to HIV-1 emphasize the importance of human leukocyte antigen-DQ and CD4 in anti-HIV-1 immunity.