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HLA-B Bw4 AND Bw6 ALLELES AND RISK FOR HIV-1 TRANSMISSION IN HIV-SERODISCORDANT HETEROSEXUAL COUPLES

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BACKGROUND: Sex between men and women is the most common mode of HIV-1 transmission worldwide. The risk of sexual transmission is highly variable and genetic factors may play a role. Because HLA-B alleles influence HIV-1 disease progression, they might also influence HIV transmission. Particularly, HLA-B Bw4 alleles have a protective influence on the rate of progression to AIDS. In this study, we investigated if presence of HLA-Bw4 alleles in HIV-1-infected men with hemophilia decreased the risk for HIV-1 transmission to their female sex partners.

METHODS: The study population consisted of 312 HIV-infected men enrolled into the Multicenter Hemophilia Cohort study and their 335 female sex partners. Blood from study participants was collected at each study visit. Data were obtained from clinical records and questionnaires. HLA was typed using sequence-specific primers flanking exons 2 and 3. PCR products were blotted on nylon membranes and hybridized with sequence-specific oligonucleotide probes. Statistical analyses were based on 335 couples. We calculated odds ratios (OR) and 95% confidence intervals (95% CI) to compare the proportions of women that were infected with HIV-1 according to the Bw4/Bw6 genotype of their male sex partner. We compared the fit of alternative genetic models with a likelihood ratio test.

RESULTS: Among the 335 women, 45 (13.4%) were infected with HIV-1. The proportion of women that were infected with HIV-1 differed by the Bw4/Bw6 genotype of the man: Bw6/Bw6, 23/120 (19.17%); Bw4/Bw6, 18/161 (11.18%); Bw4/Bw4, 4/54 (7.41%). In an "allele dose" model the risk of transmission was inversely related to the number of Bw4 alleles carried by the HIV-infected men (one Bw4 allele: OR=0.56, 95% CI [0.34, 0.92]; two Bw4 alleles, OR=0.31, [0.12-0.84]; p=0.02). In a dominant

genetic model, men who carried the Bw4 allele were about half as likely to transmit HIV-1 to a female sex partner (OR 0.48, 95%CI [0.26-0.91], p=0.02) as men who had two copies of Bw6. We could not differentiate between these alternative genetic models.

CONCLUSIONS: The presence of HLA-Bw4 alleles in HIV-1-infected men was associated with a decreased risk of HIV transmission from HIV-positive men to their female sex partners. It might be possible that HLA-B Bw4 allele carriers have a decreased seminal HIV RNA load which leads to a decreased HIV-1 transmission risk.

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