Abstract:

A small group of women (n = 80) within the Nairobi-based Pumwani Sex Workers Cohort demonstrates epidemiologic resistance to HIV-1 infection. Chemokine receptor polymorphisms and β-chemokine overproduction have been among the mechanisms suggested to be responsible for resistance to HIV-1 infection. This study attempts to determine if any of those mechanisms are protecting the HIV-1-resistant women. Genetic analysis of CCR5 and CCR3 from the resistant women demonstrated no polymorphisms associated with resistance. Expression levels of CCR5 among the resistant women were shown to be equivalent to that found in low-risk seronegative (negative) controls, while CXCR4 expression was greater among some of the resistant women. In vitro infection experiments showed that phytohemagglutinin (PHA)-stimulated peripheral blood mononuclear cells (PBMCs) from resistant women were as susceptible to infection to T cell- and macrophage-tropic North American and Kenyan HIV-1 isolates as were the PBMCs from negative controls. No significant difference in circulating plasma levels of MIP-1α and MIP-1β were found between the resistant women and negative or HIV-1-infected controls. In vitro cultures of media and PHA-stimulated PBMCs indicated that the resistant women produced significantly less MIP-1α and MIP-1β than did negative controls and no significant difference in RANTES levels were observed. In contrast to studies in Caucasian cohorts, these data indicate that CCR5 polymorphisms, altered CCR5 and CXCR4 expression levels, cellular resistance to in vitro HIV-1 infection, and increased levels of β-chemokine production do not account for the resistance to HIV-1 infection observed among the women of the Pumwani Sex Workers Cohort