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Oral presentation

S011-05 OA. HLA-A*7401 is associated with protection from HIV-1 acquisition and disease progression in Mbeya, Tanzania

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Background

Genetic variation in class I HLA impacts the strength, breadth, and depth of anti-HIV adaptive cellular immune responses, while also influencing innate immunity via interaction with killer immunoglobulin receptors (KIR) on natural killer (NK) cells. Allele HLA-A*7401 is found almost exclusively in sub-Saharan African populations with little known about the immune responses it restricts. The objective of this exploratory study was to investigate the effects of HLA-A*7401 on disease progression and risk of HIV-1 acquisition in an East African cohort population.

Methods

3,096 consented adults were enrolled in a prospective cohort in Mbeya, Tanzania with semiannual follow-up for 42 months. Studied individuals included: HIV sero-prevalent at enrollment (n = 508), HIV sero-converters (n = 99) and individuals remaining sero-negative (n = 174). Class I HLA was genotyped using a high-throughput high-resolution real-time PCR-based platform. CD4-cell counts were determined cross-sectionally for sero-prevalent individuals at enrollment. Genetic and statistical analyses were performed using PyPop and JMP.

Results

HLA-A*7401 carriers (13.8%) had a decreased risk of HIV-1 acquisition compared to non-carriers (O.R. = 0.39; 95% C.I. = 0.17–0.88; p = 0.02). HLA-A*7401 showed no significant effect on viral load set-point (p = 0.57). Among HIV sero-prevalent cases, HLA-A*7401 was associated with protection from disease progression (CD4-counts<200 cells/ul) (O.R. = 3.91; 95% C.I. = 1.39–11.03; p = 0.002; age-adjusted O.R. = 4.11; 95%C.I. = 1.62–13.87; p = 0.002). This association remained significant after controlling for linkage disequilibrium with HLA-B and HLA-C alleles.

Conclusion

The protection from HIV acquisition and disease progression conferred by HLA-A*7401 in this exploratory study could be due to direct and/or indirect effects. HLA-A*7401 could be directly involved in NK-mediated innate immune responses through interaction with KIR. Additionally, HLA-A*7401 may restrict adaptive immune responses to an unknown pathogen, thus diminishing the level of immune activation, and indirectly protecting from HIV acquisition and disease progression. The implications of these results on the design and evaluation of preventive vaccines warrant further study to elucidate the involved protective mechanisms.