

A Trim5alpha Exon 2 Polymorphism is Associated with Protection from HIV-1 Infection in Pumwani Sexworker Cohort

Abstract:

Objective The innate immune component TRIM5 α has the ability to restrict retrovirus infection in a species-specific manner. TRIM5 α of some primate species restricts infection by HIV-1, while huTRIM5 α lacks this specificity. Previous studies have suggested that certain polymorphisms in huTRIM5 may enhance or impair the proteins affinity for HIV-1. This study investigates the role of TRIM5 polymorphisms in resistance/susceptibility to HIV-1 within the Pumwani sex worker cohort in Nairobi, Kenya. A group of women within this cohort remain HIV-1 seronegative and PCR negative despite repeated exposure to HIV-1 through active sex work. Design A 1 kb fragment of Trim5alpha gene, including exon 2, from 1032 women enrolled in the Pumwani sex worker cohort was amplified and sequenced. SNPs and haplotypes were compared between HIV-1 positive and resistant women. Methods The TRIM5 exon 2 genomic fragment was amplified, sequenced and genotyped. Pypop32-0.6.0 was used to determine SNP and haplotype frequencies and statistical analysis was carried out using SPSS-13.0 for windows. Results A TRIM5 SNP (rs10838525) resulting in the amino acid change from Arginine to Glutamine at codon 136, was enriched in HIV-1 resistant individuals ($p=1.104E-05$; OR:2.991; CI95%:1.806–4.953) and women with 136Q were less likely to seroconvert ($p=0.002$; Log Rank: 12.799). Wild type TRIM5 α exon 2 was associated with susceptibility to HIV-1 ($p=0.006$; OR:0.279; 95%CI:0.105–0.740) and rapid seroconversion ($p=0.001$; Log Rank: 14.475). Conclusions Our findings suggest that a shift from arginine to glutamine at codon 136 in the coiled-coil region of TRIM5 α confers protection against HIV-1 in the Pumwani sex worker cohort. Keywords: TRIM5 α , Single nucleotide polymorphism, HIV-1, Sex Workers, Taxonomy-based Sequence Analysis, Disease Association, Disease Resistance