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HTLV-2 Induces Resistance to CCR5-Dependent HIV-1 Infection Via Selective PBMC Expression of CCL3L1

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Background

In HIV-1/HTLV-2 co-infected IDUs the CCL3/MIP-1alpha induction by HTLV-2 leads to HIV inhibition. *CCL3* gene codes for CCL3/LD78alpha and CCL3L1/LD78beta isoforms. CCL3L1 binds more potently to CCR5 than any other chemokine. Possession of a *CCL3L1* copy number lower than two (the population average for Europeans) is associated with markedly enhanced HIV/AIDS susceptibility. Here, we analysed the genotype frequency of *CCL3L1* and its expression in 8 HTLV-2-infected/HIV-1-exposed-seronegative (HTLV-2/HIV-1^{ESN}) individuals, 7 LTNP-HIV-1/HTLV-2-co-infected and 8 LTNP-HIV-1-mono-infected subjects.

Methods

R5 HIV-1 infection of PBMC from HTLV-2/HIV-1^{ESN} was evaluated for HIV proviral load and for p24 production. *CCL3L1* gene copy number and mRNA expression levels were assessed using real-time PCR. CCL3 and CCL3L1 isoforms were identified from spontaneous PBMC cultures by mass spectrometry (MS).

Results

R5 infectibility and efficiency of viral replication in primary PBMC from HTLV-2/HIV-1^{ESN} were very low. The median of CCL3L1 copy number was one in HTLV-2/HIV-1^{ESN}, three in LTNP-HIV-1 and two in HIV-1/HTLV-2 subjects. *CCL3-L1* mRNA was more abundant in individuals with HTLV-2 infection than in HIV-1 LTNPs. MS analysis evidenced that intact CCL3L1, usually not secreted from healthy subjects, was produced by PBMC of HTLV-2/HIV-1^{ESN}. Noteworthy, CCL3L1 isoform was highly expressed by PBMC of LTNP HIV-1/HTLV-2, but not of HIV-1 LTNPs. The high CCL3L1 production, and a persistent IFN-gamma secretion, conferred a CCR5^{low} phenotype to HTLV-2 infected subjects.

Conclusion

HTLV-2 may curtail HIV-1 infection upregulating the CCL3L1/LD78beta chemokine. Apparently, HTLV-2 infection can fully compensate for the functional state conferred by CCL3L1^{low}.