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Decreased interferon signature in HIV-1 viremic controllers

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Background: Several host-encoded interferon-inducible antiviral factors suppress HIV-1 replication in a cell-autonomous fashion in vitro. The relevance of these defences to the control of HIV-1 in vivo in humans remains to be elucidated. Recent data from Sandler et al. suggest that administration of interferon to monkeys, and hence the modulation of restriction factor expression at different stages of SIV infection dramatically determines disease outcome. We hypothesized that host restriction factors play a role in disease outcome in chronically HIV-1-infected individuals.

Methods: A total of 99 chronic HIV-1-infected individuals were selected from the cohort at the National Institute of Respiratory Diseases in Mexico City and divided into 3 groups: 1) Low Viremic (VL < 2,000 copies and CD4 >250), 2) High Viremic (VL >10,000 copies and CD4 >250) and 3) Advanced Infection (VL >10,000 copies and CD4 < 250). Twenty HIV-1-uninfected individuals from the same ethnic background were used as a control group. CD4+ T cells were enriched from whole PBMC and the expression of 42 established anti-HIV-1 genes was determined by quantitative real-time PCR.

Results: We consistently detected an overexpression of restriction factors and ISGs in individuals with advanced disease, followed by high viremic individuals ($p < 0.0001$, Krustal-Wallis Test). Low viremic individuals had the lowest expression, even compared to uninfected. The expression of IFITM1, RTFI, TRIM22, RSAD2/Viperin and SLFN11 significantly correlated with VL in individuals with advanced infection ($r > 0.43$, $p < 0.05$). Finally, we performed 4-digit HLA typing and found unconventional HLA-B haplotypes to be associated with either control (B*3902) or risk (B*3905) of HIV-1 disease and restriction factor expression profile.

Conclusions: In conclusion, we show evidence for the existence of novel mechanisms associated with protection or risk of HIV disease progression in a previously uncharacterized population with unique immunogenetic characteristics.