

Poster presentation

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## P08-01. Heme oxygenase-1 promoter polymorphisms correlate with favorable virologic and immunological parameters in HIV-1 infection

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### Background

Since high levels of immune activation are predictive of progressive HIV disease, host immunoregulatory factors that blunt immune activation may contribute to delayed disease progression. Heme oxygenase-1 (HO-1), the rate-limiting enzyme in heme catabolism, is a potent anti-inflammatory protein that may represent one such factor.

### Methods

We hypothesize that efficient up-regulation of HO-1 in response to HIV-1 infection is associated with more favorable clinical outcomes. To address this hypothesis, we conducted a candidate genotyping study of HO-1 promoter polymorphisms that are known to influence the magnitude and rapidity of HO-1 gene expression: a microsatellite (GT)<sub>n</sub> repeat and two single nucleotide polymorphisms (-1135 A/G) and (-413 A/T). Specific alleles of these genes have previously been shown to favor enhanced HO-1 gene expression and to correlate with favorable outcomes in non-HIV inflammatory diseases. Two patient groups were identified from the HIV-1 SCOPE cohort: elite controllers with no detectable viremia (n = 47) and non-controllers with viral loads > 10,000 (n = 218) in the absence of HAART.

### Results

There was an enrichment of the HO-1 (-1135A) allele in Caucasian elite controllers compared to non-controllers

(p < 0.009). We also observed that, among elite controllers, there was an association between the presence of the protective short (GT)=26 microsatellite repeat and lower levels of CD8+ T cell activation, as measured by surface staining of CD38 (p = 0.049). Haplotype analysis revealed a statistically significant enrichment of a specific haplotype [-1135(G), -413(A), GT>26] in the non-controller cohort (p = 0.04).

### Conclusion

Our study demonstrates that Caucasian HIV-1 patients who maintain low levels of immune activation and control viral loads to undetectable levels are more likely to possess HO-1 promoter polymorphisms that favor enhanced HO-1 gene expression. These results suggest that efficient induction of HO-1 may play a role in limiting HIV-induced immune activation in the host, resulting in less immune dysfunction and better clinical outcomes.