

## ORAL ABSTRACT SESSION 08: INNATE AND MUCOSAL IMMUNITY

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## HIV-1 elite controllers resist HIV-1 infection via p21 (cip-1/waf-1)

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**Background:** Elite controllers are a small population of HIV-1 infected persons with undetectable viremia in the absence of antiretroviral therapy. These individuals with a “functional cure” of HIV-1 infection may serve as a model for successful host immune activity against HIV-1, but correlates of immune protection in this patient population are ill defined.

**Methods:** HIV-1 replication steps in CD4 T cell from elite controllers, HIV-1 negative persons, HIV-1 progressors and HAART-treated patients were analyzed after ex vivo infection with a VSV-G pseudotyped HIV-1 vector or primary HIV-1 isolates, using established PCR assays to quantify extra- and intrachromosomal HIV-1 DNA and HIV-1 mRNA. p21 gene expression was analyzed by RT-PCR and western blots in quiescent (HLA-DR-) and activated (HLA-DR+) CD4 T cells from elite controllers, and reference populations. Functional HIV-1 infection assays were performed in the presence or absence of a small molecule inhibitor of p21.

**Results:** CD4 T cells from elite controllers were significantly less susceptible to HIV-1 infection in comparison to reference patient cohorts ( $p < 0.01$ ). This resistance was due to less effective reverse transcription and HIV-1 mRNA transcription from proviral DNA. Defective viral replication in elite controllers corresponded to significant ( $p < 0.001$ ), 10- to 20-fold higher expression levels of p21 in cells from elite controllers compared to the reference populations. In ex vivo infection assay, blockade of p21 significantly ( $p = 0.01$ ) enhanced reverse transcription and HIV-1 mRNA transcription in CD4 T cells.

**Conclusion:** These data indicate that the selective upregulation of p21 represents a natural barrier against HIV-1 reverse transcription and mRNA transcription in CD4 T cells from elite controllers, and significantly contributes to the ability of elite controllers to maintain undetectable viral replication. Manipulation of p21 may provide novel opportunities to increase host resistance to HIV-1 infection.