Retrovirology

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Oral presentation

Negative regulation of HIV-1 expression by the natural isoform C-terminus truncated STAT5 (STAT5Δ)

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We have described a constitutive activation of naturally C-terminus truncated STAT5 (STAT5Δ) in PBMC of most HIV+ individuals (C. Bovolenta, Blood, 1999). We here report that the chronically HIV-infected promonocytic cell line U1 expresses exclusively a STAT5Δ isoform similar to that of PBMC of HIV+ individuals in virtual absence of STAT5FL. Consistently with the presence of functional STAT5 DNA binding sites in the HIV-1 LTR (Selliah et al., Virology, 2006), GM-CSF stimulation of U1 cells led to a modest induction of HIV expression as well as to the activation of both STAT5Δ and of an ERK-1/2-AP-1 pathway. Inhibition of ERKs/AP-1 by PD98059 abolished GM-CSF induced HIV expression in U1 cells, whereas inhibition of STAT5Δ expression by either AG490 or anti-STAT5 siRNA resulted in a significant enhancement of GM-CSF induced HIV expression in U1 cells. Finally, ex vivo IL-2 stimulation of PBMC from most HIV+ individuals in the presence of anti-STAT5 siRNA resulted in the enhancement of HIV-1 p24 Gag antigen expression. Thus, STAT5Δ is likely a novel natural inhibitor of HIV expression both in vitro and in vivo.