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***In Vivo* Assessment of Antiviral Reactivity in Chronic HIV Infection**

K.A. Smith¹, E.L. Jacobson¹, T. Sohn¹, D. Warren², R. Emert¹, M. Giordano³, A. M. Dunne¹, and M. Lobo¹.

¹ Weill Medical College of Cornell University, ² SUNY, Brooklyn, NY, ³ Smith Kline Beecham, Waterbury, CT.

Background: Chronic infection with HIV renders individuals deficient in their capacity to recognize and react to HIV as defined by *in vitro* assays.

Methods: To determine whether *in vivo* antiviral reactivity is detectable in chronic HIV infection, viral and lymphocyte dynamics were monitored twice weekly after supervised treatment interruption (STI). Chronically infected (> 6 months) subjects were eligible to interrupt antiviral therapy if there was an undetectable plasma [HIV] (< 50 RNA/mL) and normal [lymphocyte] while receiving antiviral therapy and daily low dose subcutaneous interleukin 2 (IL2, 1.2 mU/M² BSA) for at least 3 months. IL2 was continued after STI.

Results: Twenty-nine (29) subjects have entered study, 14 subjects have undergone 1 STI, and 6 have undergone 2 STIs. All subjects underwent a viral relapse upon the 1st STI. Data from the 1st 9 subjects revealed a mean time to relapse of 19 +/- 3 (SEM) days, and a doubling time of 1.6 +/- 0.2 (SEM) days. Plasma [HIV] peaked within 17 +/- 2 (SEM) days at 5.15 +/- 0.21 (SEM) log₁₀ HIV RNA/mL. Subsequently, plasma [HIV] decreased with a t1/2 of 3.5 +/- 0.7 (SEM) days to 4.21 +/- 0.19 (SEM) log₁₀ HIV RNA/mL within 8 weeks from STI. The difference between the peak and trough (4 successive values < 25% of the mean) [HIV] was significant (p < 0.001, two-tailed T test). Coincident with the decline in plasma [HIV] was a transient, 24% decrease of CD4+ T cells, while CD8+ T cells doubled (p < 0.01, paired T test) and remained elevated until antiviral therapy was reinitiated. The mean time off antiviral therapy after the 1st DTI was 120 days (range 44-288 days). Subsequent to the 2nd STI, the peak plasma [HIV] was => 10-fold lower than the 1st in 5/6 subjects, and the mean [HIV] remained , 20,000 RNA/mL in 4/5 subjects for a mean of 194 days (range 92-330 days).

Conclusions: Monitoring viral & lymphocyte dynamics after STI readily detects host antiviral reactivity in chronic HIV infection. Therefore, studies that explore immunotherapies designed to augment antiviral host reactivity are now warranted prior to STI, to test their capacity to prevent or attenuate the viral relapse.