Relationship Between CCR5 Density and Viral Load After Discontinuation of Antiretroviral Therapy

To the Editor: Discontinuation of combined antiretroviral therapy (CART) improves virological control and specific immunity in some persons infected with human immunodeficiency virus 1 (HIV-1), whereas in others it results in rapid viral rebound and decrease in the antiviral cytotoxic T cell responses below the pretherapeutic level. The host factors responsible for these opposite consequences are largely unknown. We have recently reported that the mean number of CCR5 coreceptors at the surface of CD4 T cells (CCR5 density) is logarithmically correlated with viral load and disease progression during HIV-1 infection. We have explained this link by showing in vitro that CCR5 density strongly determines the efficiency of HIV-1 life cycle, particularly at the reverse transcription stage. Herein we report a test of the hypothesis that CCR5 density, which is stable over time in a given individual but varies among individuals, might determine the intensity of viral rebound after cessation of CART.

Methods. We used quantitative flow cytometry to measure CCR5 density on peripheral blood CD4 T cells of all chronically infected patients in our clinic who stopped antiretroviral multi-therapy in an 18-month period because of physical or psychological drug intolerance (8 women and 15 men). All had CD4 T cell counts ranging from 300 to 1739 and HIV-1 RNA plasma levels below 200 copies/mL. We also measured virus load at day 30 after discontinuation of CART.

Results. The Figure shows a strong logarithmic relation (r = 0.644, P = .001) between CCR5 expression and plasma level of HIV-1 RNA. Interestingly, beyond a threshold of 8000 CCR5 molecules per CD4 T cell, virus load rebounded above 100 000 copies/mL.

Comment. These results emphasize the notion that CCR5 density is related to in vivo virus production and may explain why virus loads before CART and after cessation of CART are comparable. Moreover, they suggest CCR5 density as a predictive factor of the effect of treatment interruption, and emphasize the possible therapeutic potential of agents that would antagonize CCR5.

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CORRECTION

Incorrect Units: In the Original Contribution entitled “Effect of Magnetic vs Sham-Magnetic Insoles on Plantar Heel Pain: a Randomized Controlled Trial” published in the September 17, 2003, issue of The Journal (2003;290:1474-1478), some data were reported with incorrect units. In Table 1, the mean (SD) duration of pain should have been reported, not in months, but in weeks (ie, 120 [170] weeks in the nonmagnetic insole group and 85 [86] weeks in the magnetic insole group).