LETTER

Frequency of apolipoprotein E4 among older compared with younger HIV patients: Support for detrimental effect of E4 on survival

We read with interest a recent article by Burt *et al*. demonstrating accelerated HIV disease course with apoE4 (1). This finding is congruent with data from the Hawaii Aging with HIV Cohort (HAHC). We previously completed apoE genotyping among 222 HAHC enrollees, 103 of whom were <40 years old (younger cohort) and 119 of whom were at least 50 years old (older cohort). Here, apoE4 conveyed risk for research-designated HIV-associated dementia (HAD) within the older group but not the younger group (2). We were intrigued by the fact that having an apoE4 allele was less frequently noted in our older group (23%) compared with our younger group (37%, $P = 0.020$). Our younger group is more ethnically diverse, possibly accounting for some differences; however, this trend remained when analyzed among only Caucasian enrollees [22% older ($n = 83$), 38% younger ($n = 40$), $P = 0.064$]. We speculated that selection bias may be present or that apoE4 could influence survival, a conviction that seems more apt in light of these new data.

HAHC individuals with at least one apoE4 tend to have a shorter self-reported HIV duration (10.5 vs. 8.3 years, $P = 0.012$), even when analyzed separately among only older enrollees (12.6 vs. 9.8 years, $P = 0.014$). Among older individuals diagnosed before antiretroviral therapy was available (1988), only 7/45 (16%) have at least one apoE4 allele. Study entry CD4 lymphocyte count and plasma HIV RNA levels did not differ by apoE4, and we do not identify differences in intracellular (peripheral mononuclear cell) HIV DNA by E4 status, a robust marker of HAD in this cohort (37 vs. 25 copies per 10^6 cells, $P = 0.551$) (3).

ACKNOWLEDGMENTS. This work was supported by Grants 1U54NS43049 and NS053345 (National Institute of Neurological Disorders and Stroke/National Institutes of Health, Bethesda).

Victor Valcour*, Bruce Shiramizu, and Cecilia Shikuma
Hawaii AIDS Clinical Research Program, University of Hawaii at Manoa, Honolulu, HI 96816

1. Burt TD, *et al*. (2008) Apolipoprotein (apo) E4 enhances HIV-1 cell entry *in vitro*, and the *APOE* ε4/ε4 genotype accelerates HIV disease progression. *Proc Natl Acad Sci USA* 105:8718–8723.
2. Valcour V, *et al*. (2004) Age, apolipoprotein E4, and the risk of HIV dementia: The Hawaii Aging with HIV Cohort. *J Neuroimmunol* 157:197–202.
3. Shiramizu B, *et al*. (2005) Circulating proviral HIV DNA and HIV-associated dementia. *AIDS* 19:45–52.

Author contributions: V.V., B.S., and C.S. wrote the paper.

The authors declare no conflict of interest.

*To whom correspondence should be addressed. E-mail: vvalcour@hawaii.edu.