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LOWER RATES OF ADAPTIVE EVOLUTION IN HIV-1 DUAL INFECTIONS COMPARED TO SINGLE INFECTIONS

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INTRODUCTION: HIV-infected individuals who harbour two phylogenetically distinct strains of HIV-1 (dual infection), early in infection, appear to progress more rapidly to disease. The mechanism by which this occurs has not been elucidated. We investigated whether viruses from individuals with dual infection evolved more rapidly than viruses from individuals with single infection, and if so, whether the primary mechanism of diversification was through point mutations or recombination.

METHODS: Sequences from randomly sampled clones, collected over time, were analyzed to compare the rates of adaptation through point mutation between viral populations from individuals with dual infection ($n=6$) and individuals infected with a single strain (single infection, $n=8$). Estimates of rates of adaptation were determined using a modified version of the McDonald Kreitman test which was adapted for use with divergent and recombining sequences. Full-length sequences from one dually infected individual were generated.

RESULTS: The rate of adaptation through point mutation was significantly lower in the dual infections compared to single infections: 1.67×10^{-4} mutations per month per site rose to high frequency or were fixed in the dual infection through positive selection compared to a rate of 4.48×10^{-4} for the single infections ($p=0.03$). Recombination was evident in all dually infected individuals. Analysis of near full-length genomes generated from a dually infected participant with rapid disease progression at time points 2, 9 and 17 months post infection suggested evasion of cellular and antibody immune pressure through recombination.

CONCLUSIONS: We hypothesize that the increased viral diversity in dual infection enables recombination to contribute significantly to viral adaptation to immune responses and that this results in a decrease in the rate of adaptation affecting individual point mutations. The ability to undergo major genetic shift in viral populations may help to explain rapid disease progression in individuals with dual infection.

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Viral dynamics and fitness | MoFo0305 | C. Williamson
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