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## DIMINISHED REPRESENTATION OF HIV-1 VARIANTS HARBOURING M184V MUTATIONS IN PRIMARY HIV INFECTION (PHI)

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**OBJECTIVES:** Previous findings, using population-based genotyping, showed the potential for reduced transmissibility of viral variants harbouring M184V mutations compared with other mutations associated with HIV drug resistance (Turner DJ, *et al.*, [Acquir Immune Defic Syndr.](#) 2004 Dec 15;37(5):1627-31). However, this work was subject to the criticism that viruses containing M184V had simply been overgrown by revertants or by wt viruses transmitted in the quasispecies. Therefore, the current study employed ultrasensitive assays to detect minority species and also included 3TC selections *in vitro* to further substantiate our findings.

**METHODS:** Sequencing data from the Quebec PHI cohort and the provincial genotyping surveillance program established the frequency of drug resistance mutations in PHI as compared to potential transmitter (PT) study populations of treated patients harbouring resistance. Sequential plasma samples of PHI cases with transmitted resistance were analysed by M184V allele specific real-time PCR as described by Palmer *et al* ([AIDS.](#) 2006 Mar 21;20(5):701-10). In select cases, PHI viruses were isolated and selected *in vitro* with lamivudine (3TC) and other drugs.

**RESULTS:** Our surveillance data show lower representation of M184V in PHI ( $n=59$ ) versus PT ( $n=380$ ) populations (ratios of 1:7, 1:4, and 1:3, respectively) in comparison with TAMs (thymidine analogue mutations), non-nucleoside mutations (NNMs) and PI mutations. Allele specific real-time PCR failed to detect M184V in PHI cases harbouring transmitted 215Y/F/D/N/C/S, TAMs, NNMs, and PI mutations (<1% of quasispecies with a 0.2% cutoff). In contrast, routinely genotyped samples from patients on treatment interruptions who harboured TAMs, NNMs or PI mutations but not M184V contained M184V minority species in about one-third of cases by real-time PCR. In addition, 3TC

selections of PHI isolates harbouring TAMs, NNMs or PI mutations, without M184V, did not expand M184V over 3 weeks of culture, whereas continued exposure of these stocks did select M184V after 9–12 weeks.

**CONCLUSIONS:** The reduced transmissibility of M184V in PHI is not simply explained by rapid deselection of M184V or by the presence of less fit M184V minority species. These studies support the concept that viruses containing M184V may be negatively impacted in regard to transmission fitness as well as replication competence.

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