DEEP SEQUENCE ANALYSIS OF HIV ADAPTATION FOLLOWING VERTICAL TRANSMISSION REVEALS THE IMPACT OF IMMUNE PRESSURE ON THE EVOLUTION OF HIV

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Background: Human immunodeficiency virus (HIV) is responsible for more deaths than any other infectious disease worldwide, with the only treatment option being lifelong antiretroviral therapy. HIV adapts to an individual's T-cell immune response via genomic mutations that affect antigen recognition and impact disease outcome. These viral adaptations are specific to the host's human leucocyte antigen (HLA) alleles, as these molecules determine which peptides are presented to T-cells. Furthermore, these adaptations can be transmitted. To design an effective vaccine, it is vital to understand the complex host-viral interactions. In this study, we predict the in vivo replicative cost and immune benefit of specific HIV adaptations and assess specific T-cell responses.

Methods: We utilised a deep sequencing approach to determine HIV quasispecies in 26 mother/child transmission pairs. The resultant sequences and previously determined viral adaptations were used to determine adaptations present, and corresponding adaptation scores for the transmitted virus using in house bioinformatic tools.

Results: We showed that the pattern of reversion/fixation of HIV adaptations following transmission provides insight into the replicative cost associated with specific adaptations in vivo. Transmitted viruses were commonly pre-adapted to the child's HLA genotypes across the cohort, however we found evidence of de novo post-transmission adaptation. The T-cell responses in the child overall suggested the immune response to pre-adapted HIV strains may focus on sub-dominant T-cell epitopes.

Conclusion: High-resolution sequence analysis revealed intra-host reversion and maintenance dynamics of transmitted adaptations in different immune selection environments, which acts as an estimate of the replicative cost and immune benefit of specific adaptations in vivo. It is hoped a better understanding of these dynamics can be used to inform vaccine design.

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