

Poster presentation

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P20-12. Heterogeneity of Gag mutational pathways in primary HIV-1 subtype C infection

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Background

Questions addressed in this study included: "What Gag mutations are most frequent in primary HIV-1C infection?", "When do these mutations occur in relation to the estimated time of seroconversion?", and "How are these mutations associated with MHC class I HLA alleles?"

Methods

A total of 42 subjects (8 acutely and 34 recently HIV-infected individuals with estimated time of seroconversion) were included. Gag quasispecies were analyzed by single-genome amplification/sequencing. Ten amino acid positions across Gag with the most frequent mutations were chosen for analysis. Mutations were analyzed at frequent time points (median 4.5 per subject; IRQ 3.0; 6.0). High-resolution typing was performed within HLA-A, -B, and -C loci. Gag mutations toward the wild type were treated as reversions and mutations from the wild type as escapes. Mutations were classified as minor, transient, dominant, or complete.

Results

The most frequent mutations were found in p17 (position 28), p24 (positions 242, 269), and p2/p7/p1/p6 (positions 370, 411, 428, 431, 449, 459, 471). Most of the observed Gag mutations fit or could be explained by previously described CTL/CD8+ epitopes, although MHC class I HLA alleles expressed by analyzed subjects did not

necessarily match previously reported HLA restriction. Timing and patterns of viral mutations at position 242 matched clearly with the presence or absence of HLA-B*57/5801. A high frequency of transient mutations in Gag was evident at positions 28, 431, 449, and 471, where the observed mutations were minor or were lost soon after appearance.

Conclusion

Distribution of Gag mutations revealed the dominance of the most frequent Gag mutations within p2/p7/p1/p6, which was in line with the viral diversity within Gag cleavage products. Analysis of MHC class I HLA alleles implied broader HLA restriction of involved CTL/CD8+ epitopes. The transient nature of many observed mutations in Gag suggested their lower fitness, apparently due to structural and functional constraints.