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Poster presentation

P09-09. Impact of immune-driven sequence variation in HIV-1 subtype C Gag-Protease on viral fitness and disease progression

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Background

Control of HIV replication is determined by a complex interaction of viral genetic, host genetic and immune factors, the understanding of which is crucial to developing an effective vaccine. In some studies, HIV Gag immune responses correlate with low viral loads and it is hypothesised that some HLA alleles select for escape mutations in conserved Gag epitopes, resulting in a fitness cost. We are investigating the impact of HLA-driven variation in Gag on fitness and disease progression in a population of 451 HIV-1 subtype C infected individuals.

Methods

Gag-Protease NL43 recombinant viruses were generated by electroporation of a green fluorescent protein reporter cell line with plasma-derived gag-protease PCR products and pNL43Δgag-protease. The replication capacities of recombinant viruses were determined by calculating the slope of increase in percentage infected cells, as measured by flow cytometry, from days 3–6 following infection.

Results

254 recombinant viruses have been generated and replication capacities determined for 115. Preliminary analysis shows that overall there is no correlation between viral load/CD4 count and fitness. However, the least fit viruses (0.37–0.5, n = 14) were associated with lower viral loads (Mann-Whitney, p = 0.009) but not significantly higher CD4 counts when compared with those displaying high fitness (0.75–0.94, n = 12). No statistically significant associations were found between previously described protective HLA types and fitness.

Conclusion

We have set up a system to measure the influence of subtype C Gag-Protease variability on fitness and generated a means to further characterise functional consequences of genetic variation. Preliminary results suggest that Gag-Protease sequence variation can significantly impact on viral fitness and that this may in turn have clinical significance. More data may be required to test whether HLA alleles influence Gag-Protease function at population-wide level in HIV-1 subtype C infection.