Retrovirology

Poster presentation

P07-06. HIV-1 transmission and early evolution: whole genome analysis

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Background

Understanding the initial events occuring after transmission of HIV-1 to a new host is key to determining the requirements for protective immunity.

Methods

We studied nine individuals in acute HIV-1 infection (starting in Feibig stages I or II), including four index:seroconverter partner pairs, with 10 or more viral whole genome sequences collected at serially sampled visits (up to 12) for up to one year after infection.

Results

Comparison between index and seroconverter sequences showed that the dominant HIV-1 variant in the index partner was not necessarily the founder variant in the seroconverter. While HIV-1 infection was established by 2 variants in 2 individuals, 7 individuals presented single founding variants, which showed remarkably homogeneous viral population at the earliest time-points. Intrapatient viral diversity accumulated gradually in all individuals. Given the rapid population growth that occurs in acute infection, and the subsequent decline in this population at the time of seroconversion, we tested for deviations from neutral evolution and found that the earliest time-points were more likely to deviate from apparent neutrality. Cytotoxic T Lymphocyte (CTL) pressure was manifest over the whole proteome and predominantly visible in variable proteins, Env and Nef in particular. Longitudinal analyses showed mutations becoming consensus – as early as day 21 in Tat – and complete displacements of epitopes found at baseline – as early as day 53 in Env. Overall, we found more evidence of escape mutations than reversions.

Conclusion

We showed that a single viral variant establishes infection in most successful transmissions and that the dramatic CD4 T-cell depletion and viral population expansion observed in acute infection leave signature traces on the viral sequence population. We also found that the evolutionary response of HIV-1 to CTL pressure is early, complex, and dominated by escape mutations, while reversions might play a lesser role than previously thought.