Continuous evolution of HIV-1 more than ten years after infection in an elite neutralizer

Antoine Chaillon, Martine Braibant, Stéphane Hué, Samia Bencharif, Moreau Alain, David Enard, Assia Samri-Hassimi, Henri Agut, Francis Barin

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A Chaillon[1*], M Braibant[2], S Hué[3], S Bencharif[2], A Moreau[2], D Enard[4], A Samri[5], H Agut[6], F Barin[2]

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Background

The viral evolution of HIV-1 and its escape to autologous neutralizing antibodies (Nabs) during the early years of infection have been analyzed in depth. In contrast, little is known about neither the long-term evolution of the virus in patients who developed broadly Nabs (bNabs) nor the mechanism of escape in presence of these bNabs.

Methods

We have studied the viral population infecting an HIV-1 infected long term non progressor (LTNP) who had developed Nabs toward all tier 2/3 viruses (6 clades) tested, 9 years after infection, and was then followed up over 7 years. Sixty-nine env clones issued from sequential blood samples collected from 9 years to 16 years post-infection were obtained. Thirteen infectious clones representative of the genetic diversity of variants present at the different time-points were selected. Pseudotyped viruses harboring these different envelopes were generated and their sensitivity to neutralization was analyzed.

Results

Evidence of ongoing viral evolution was found, supported by both the phylogenetic analyses that showed a continuous diversification and an increasing divergence overtime. The mean autologous neutralization titers of the sequential sera toward the 13 env variants significantly increased during the period of late follow-up. The env pseudoviruses displayed a broad range of sensitivity to the autologous sera, with the most resistant variant identified at the last visit suggesting that it represented a late emerging escape variant. We identified 5 amino acids substitutions that appeared associated with escape to bNabs. They were V319I/S, R/K355T, R/W429G, Q460E and G/T463E, in V3, C3 and V5 regions.

Conclusion

This study showed that HIV-1 may continue to evolve in presence of both broadly neutralizing antibodies and increasing autologous neutralizing activity more than 10 years post-infection. Such material may provide opportunities to reveal the molecular determinants of escape of HIV-1 to highly potent broadly neutralizing antibodies.

Author details
[1]INSERM U966 Resaerch Unit, F. Rabelais University, Tours, France. [2]INSERM U966 Research Unit, F. Rabelais University, Tours, France. [3]Centre for Medical Molecular Virology, University College London, London, UK. [4]Ecology and Evolution Laboratory, CNRS UMR 7625, ENS, Paris, France. [5]INSERM U945, Pierre et Marie Curie University, Paris, France. [6]Virology Laboratory, Pitié-Salpétrière Hospital, Paris, France.

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[1]INSERM U966 Resaerch Unit, F. Rabelais University, Tours, France
Full list of author information is available at the end of the article