Rescue of long-time archived X4 minority strains and recombination to escape MVC

Baatz Franky

Retrovirology Laboratory
CRP-Santé
LUXEMBOURG
Evading Maraviroc selective pressure

Evolution of R5 viruses towards X4 viruses

Selection of minority X4 populations present before onset of treatment
**Patient 1**

- Haemophiliac, infected since mid ‘80
- Subtype B virus
- Mean VL: 107447 cp/mL (min:973, max >500000)
- Mean CD4 cell count: $<<10$ c/mm$^3$
- Under MVC (+RAL) VL became undetectable for 1 month
Genotyping and phenotyping viral populations

* Coreceptor usage was predicted by geno2pheno
Phylogenetic analysis

PhyML 3.0; γHKY model; cutoff 0.5%
Patient 2

- Subtype F1 virus
- Mean VL: 6737 cp/ml (min 50; max 54420)
- Mean CD4 cell count: 324 c/mm$^3$
- Under MVC (+RAL) VL decreased significantly (50 cp/mL)
Genotyping and phenotyping viral populations

* Coreceptor usage was predicted by geno2pheno
Phylogenetic analysis

Phylogenetic analysis

PhyML 3.0; γ HKY model; cutoff 0.5%

Pre-MVC
Plasma 2008-1
Plasma 2008-2

Post-MVC
Plasma 2008-1
Plasma 2008-2

Post-IL2 Plasma

Recco, version 0.93

www.crp-sante.lu

Presented at the 9th Eu. Workshop on HIV & Hepatitis – 25 – 27 March 2011, Paphos, Cyprus
Conclusions

• During Maraviroc treatment, even archived minority sequences that are undetectable in plasma and PBMCs at the time of treatment initiation can be rescued.

• Rescue of minority X4 strains was independant of CD4 cell counts

• Exchange of key genomic regions through recombination allowed the virus to acquire resistance patterns (X4 tropism) while maintaining the otherwise most adapted genomic context.
  → Recombination is a leap in evolution

• IL-2 boosts contributed to shaping viral evolution, diversity and persistance in different compartments.
Many Thanks to...

• Laboratory of Retrovirology, CRP-Santé
  • Danielle Perez-Bercoff
  • Jean-Claude Schmit
  • Carole Devaux
  • Morgane Lemaire
  …and the rest of the team

• FNR Luxembourg – Funding
  • Seq It GmbH
  • Martin Däumer
  • MPII, Saarbrücken
  • Alexander Thielen