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Oral presentation

Virus phenotype variability during disease progression of HIV-1 infected children

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Background

HIV-1 infected children display different clinical evolution, i.e., "fast progression" (FP), "slow progression" (SP) and "long term non progression" (LTNP). One important phenotypic trait linked to disease progression is the evolution of the viral co-receptor use [1], involving a change from CCR5 to CXCR4 use [2]. However, AIDS symptoms can appear in absence of X4 viruses. Recently chimeric receptors between CCR5 and CXCR4 were developed, in which subsequent parts of CCR5 were replaced with corresponding parts of CXCR4 [3]. Their use allowed to document the biological variability of R5 isolates during the pathogenic process in adults [4].

Aim

To examine the HIV biological variability in children with different modes of disease progression.

Materials and methods

119 isolates from19 HIV-1 positive children were tested for their ability to infect U87.CD4+ cells expressing the wild type receptor CCR5, CXCR4, or one of the 6 chimeric CCR5/CXCR4 receptors.

Results

Early during infection, all the viruses isolated from 8 SP children used only wild type CCR5 (called $R5^{narrow}$). In one case, this phenotype persisted during disease progression, whereas in 2 children the virus evolved and was able to use multiple chimeric receptors (called $R5^{broad}$), and in additional 5 children the virus evolved to CXCR4 usage. Interestingly the FP children, carried close to birth in 2 cases $R5^{narrow}$ virus, in 2 cases $R5^{broad}$ and in one case a dualtropic R5X4 virus. Virus with $R5^{narrow}$ evolved to $R5^{broad}$ in one of the 2 children carrying such phenotype. Both children with $R5^{broad}$ phenotype developed CXCR4 variants during the follow-up.

Evolution was observed also in the LTNP, although followed from later on in life (>8 years of age): all tested isolates from 2/6 LTNP remained $R5^{narrow}$ during disease progression; in one child an evolution from $R5^{narrow}$ to $R5^{broad}$ was observed whereas in another child the virus evolved from $R5^{narrow}$ to R5X4. The remaining two children showed $R5^{broad}$ phenotype during the whole follow-up.

Conclusions

Our results show that HIV-1 with broad chimeric receptor use is not hampered in transmission, and is more frequent close to birth in FP than in SP children. Viruses from LTNP show a similar phenotypic evolution though at later age.

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