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Background

CCR5 using HIV-1 variants are preferentially transmitted and have an intrinsic phenotypic variability playing an important role in AIDS pathogenesis. This variation confers a different susceptibility to CC-chemokines as well as a different capacity to infect ad hoc engineered cell lines expressing CCR5/CXCR4 chimeric receptors. In this study we explored the predictive value of R5 variability in mother-to-child transmission (MTCT) of HIV-1 and pediatric disease progression.

Methods

Virus isolates from 21 transmitting mothers and their children obtained close to birth, and 171 biological viral clones of 5 mother-child pairs were tested for their ability to infect U87.CD4+ cells expressing wild type receptors CCR5 or CXCR4, or one of the 6 CCR5/CXCR4 chimeric receptors, hybrids between CCR5 and CXCR4.

Results

The transmitting mothers carried R5X4 viruses in 5 cases, R5 broad in 10 and R5 narrow in 11 cases. The detailed analysis of the chimeric receptor usage showed that the clones of mothers with R5 broad viruses had a mixture containing also R5 narrow. To understand if a selective process occurs during transmission, we compared the viral phenotype of the mother-child couples. All 11 mothers harbouring an R5 narrow virus transmitted the same phenotype to their child. Interestingly, the 10 mothers

carrying R5 broad viruses transmitted in all but two case an R5 broad virus. The children's biological clones showed that both R5 narrow and R5 broad viruses were transmitted. The five mothers with an R5X4 transmitted the whole spectrum of virus phenotypes. The presence of R5 broad and R5X4 in the children close to birth correlated significantly with severe decline of CD4+ T cells or death within 2 years.

Conclusion

Our results show that HIV-1 with broad chimeric receptor usage are not hampered during MTCT and are predictive of disease progression. This may be of relevance for therapeutic intervention, as we showed that R5 broad viruses are less sensitive to RANTES inhibition.