A12 Transmitted HLA pre-adapted polymorphisms in the GAG protein influences viral evolution in the new host

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children through contaminated catheters and needles, and from children to mothers through breast-feeding. Since then the infection was transferred both vertically and horizontally. The source of the outbreak was the husband of one of the infected mothers who was previously infected in Congo. Before the end of 1990s, all samples of HIV subtype G in Russia were considered to originate from that outbreak. Here, we study the phylogenetics of HIV subtype G in Russia. The dataset consisted of 1,169 HIV-1 subtype G sequences of protease and reverse transcriptase, including 12 Russian sequences of unknown origin and three Russian sequences from the Elista outbreak sequenced in the Central Research Institute of Epidemiology (CRIE), and 122 sequences of Russian origin from the Los Alamos National Laboratory (LANL) HIV database (lanl.hiv.gov). Sequences were aligned with Clustal Omega, and the alignment was then manually edited in AliView. A maximum likelihood tree was reconstructed using RAxML. In the resulting phylogeny, the 120 Russian LANL sequences and the three CRIE sequences from the Elista outbreak fall into a clade nested within the sequences from Democratic Republic of Congo as expected for the 1988 Elista outbreak. By contrast, the remaining thirteen other Russian sequences, including twelve CRIE sequences and one LANL sequence, formed a strongly supported clade nested within sequences from Portugal, next to 2003–2004 sequences from Denmark. This phylogenetic evidence suggests a mixed origin of the subtype G, with a previously unreported influx of subtype G in Russia in mid-2000s from Western Europe. About eight out of twelve subtype G sequences of presumably Western European origin were later fully sequenced. Recombination analysis performed with jpHMM has shown that all of them share the same recombination with subtype B (positions 790–1,160 based on HXB2 numbering). In contrast, analysis of full-genome subtype G sequences from the Elista outbreak has not shown any recombination events. These results also support the hypothesis of mixed origin of subtype G in Russia.

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HIV escapes adaptive cellular immunity by selecting mutations that are associated with the individual's HLA-I alleles. These mutations can be transmitted and have been shown to determine disease progression in the new host but their impact on subsequent viral evolution is poorly understood. In a group of seventy-six Zambian heterosexual transmission pairs, we obtained the gag sequence at zero (donor and recipient; median $= 46$ dpi) and at three, six, nine, twelve, eighteen, and twenty-four months after infection (recipient; median $= 772$ dpi). A neighbor joining phylogenetic reconstruction of these sequences (MEGA 6.06) confirmed that the donor clustered with the corresponding recipient sequences, and showed a star-like shape in most recipients. Using both 0 months sequences, we calculated the proportion of HLA-linked sites according to the recipient's HLA alleles that harbored a mutation associated with CTL escape. We found a median of 25 per cent of pre-adapted sites and confirmed that these polymorphisms impaired immune recognition, since individuals infected with highly pre-adapted virus (>50 vs. <20 per cent) had a lower number and proportion of CTL IFN-γ responses in ELISpot assays performed

using predicted peptides ($P = 0.004$). Using the longitudinal sequences, we calculated both the rate of reversion of pre-adapted polymorphisms, which was significantly lower than that of all transmitted polymorphisms ($P < 0.0001$), and the proportion of adapted sites after two years of infection, which was significantly increased to a median of 40 per cent ($P < 0.0001$). Interestingly, the patients where the proportion of adapted sites was increased had one that was initially significantly lower ($P = 0.0014$). We also looked for evidence of adaptive evolution using the Codon-based Z-test of Selection (MEGA 6.06). We found that 50 per cent of recipients showed significant positive selection during the first two years of infection. Interestingly, female recipients that showed evidence for positive selection, excluding those expressing the B*57 protective allele, had a lower initial proportion of pre-adapted sites than those that did not show evidence for positive selection (17.7 vs. 28.6 per cent; $P = 0.06$). This study reveals that, even before an immune response is mounted in the new host, the degree of pre-adaptation of the transmitted variant determines the dynamics of viral evolution in the newly infected individual.

A13 **Social affects phylogeny: Exploration of ongoing and active transmission chains**

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In this research, we combined phylogenetic and population based statistical approaches to assess HIV transmission dynamics and identify clusters that harbor strong potential for onward transmission. Over 300 full protease and partial RT HIV-1 subtype B sequences from Serbia were analyzed. A phylogenetic tree was constructed in MEGA with 1,000 bootstrap resamplings using both a neighbor joining and maximum likelihood approach under the GTR $+$ G+I nucleotide substitution model. In addition, Bayesian estimation of phylogeny was performed using MrBayes. Identification of phylogenetic clusters was based on sets of criteria involving bootstrap support, genetic distance, Bayesian posterior probability value and Phylopart analyses. The largest transmission clusters detected were further subjected to logistic growth model (LGM) analyses implemented in the mathematical application Geogebra. The model assumed that in one year some subjects in an identified cluster were not yet diagnosed, and some had already been infected and diagnosed. Clusters were classified in three groups, as having low (<5 per cent), moderate (5–15 per cent), and high probability (>15 per cent) of hidden infection and potential for future HIV transmissions. Lastly, we examined the relationship between cluster size and socio-epidemiological profiles of cluster members. For this investigation, latent class analysis (LCA) was applied to different categorical covariates including: HIV risk factor, year of diagnosis, place of residence, education, age at diagnosis, other STIs, and clinical stage at the time of diagnosis. Phylogenetic analyses revealed the presence of fourteen transmission clusters. The majority of clustering sequences, were from male MSM patients living in Belgrade. LGM analysis of two largest transmission clusters detected, comprising thirteen and eight sequences, respectively, identified them as having very high (58 per cent) and moderate probability (10 per cent) of harboring undiagnosed infection. LCA identified four classes based on the lowest AIC that were associated with cluster size. Class 1 included high prevalence of young (20–30 years), MSM patients