from the outbreak. The present study highlighted the integral role that real-time phylogenetic analyses can play alongside extensive epidemiological investigations, assisting the clarification of epidemiological case definitions in temporal transmission network in a HIV outbreak investigation.

A25 Analysis of non-structural genes subtype A1 HIV-1 circulating in Russia

K. Gromov,[1] A. Murzakova,[2] D. Kireev,[2] and E. Kazennova[1]

[1]N.F. Gamaleya Federal Research Centre for Epidemiology and Microbiology of the Ministry of Health of the Russian Federation, Moscow, Russian Federation and [2]Central Research Institute of Epidemiology of The Federal Service on Customers' Rights Protection and Human Well-being Surveillance, Moscow, Russian Federation

The HIV infection epidemiological situation in Russia is characterized by the predominance of a unique genetic variant of subtype A1 HIV-1 named AFSU. This variant has significant differences from other subtype A1 HIV variants in the genes coding for structural proteins Gag, Pol, and Env, but no analysis of the non-structural genes was carried out. These genes may have a significant influence on the rate of viral replication and transmission, playing major role in the pathogenesis of HIV virus and interaction with the human immune system. The aim of this work was to find out if the differences in *vif*, *vpr*, *vpu*, *tat*, *rev*, and nef *genes* of AFSU variant from other subtype A1 variants exist. NGS methodology was used for the analysis of the viruses in blood plasma samples obtained from HIV-infected patients in different regions of Russia, previously identified as AFSU. We received forty-seven complete genome sequences using the MiSeq (Illumina, USA); additionally fifty-four complete genome sequences of subtype A1 HIV-1 were extracted from Genbank. All sequences were divided into fragments corresponding to vif, vpr, vpu, tat, rev, and nef genes. All sequences were subjected to phylogenetic analysis using MEGA 6.0 program. Phylogenetic analysis of vif, vpr, vpu, tat, and rev genes has shown that all AFSU samples formed a sub-cluster inside the subtype A1 cluster formed by other A1 nucleotide sequences. The *nef* gene sequences did not form any clusters irrespectively of the mode of phylogeny estimation. The results of the phylogenetic analysis showed that AFSU HIV-1 non-structural genes *vif*, *vpr*, *vpu*, *tat*, and *rev* have differences from other subtype A1 HIV-1 variants. The *nef* gene sequences did not show any phylogenetic differences. The information will be used as a background for further investigations of the epidemiological and biological characteristics of the HIV1 viruses prevailing in Russia.

A26 Probing the compartmentalization of HIV-1 in the central nervous system through its neutralization properties

K. Stefic,[1,2] A. Chaillon,[3] M. Bouvin-Pley,[1] A. Moreau,[1] M. Braibant,[1] F. Bastides,[4] G. Gras,[4] L. Bernard,[4] and F. Barin[1,2]

[1]Université François Rabelais, Inserm U966, Tours, France, [2]Laboratoire de Bactériologie-Virologie, CHU Bretonneau, Tours, France, [3]Department of Medicine, University of California San Diego, La Jolla, CA, USA and [4]Médecine Interne et Maladies Infectieuses, CHU Bretonneau, Tours, France

Compartmentalization of HIV-1 has been observed in the cerebrospinal fluid (CSF) of patients at different clinical stages. Compartment specific modifications have been frequently described in the variable loops and the glycosylation sites of the envelope glycoproteins, a known mechanism to escape neutralizing antibodies (NAb). Considering the low permeability of the blood–brain barrier, we wondered if a lower NAb selective pressure in the central nervous system (CNS) could favor the evolution of NAb-sensitive viruses in this compartment. Single-genome amplification (SGA) was used to sequence near full-length HIV-1 envelope variants (453 sequences) from paired CSF and blood plasma samples of nine subjects infected by HIV variants of different clades and suffering from neurologic syndromes. Dynamics of viral evolution were evaluated with a Bayesian coalescent approach for individuals with longitudinal samples ($n = 4$). For six subjects, pseudotyped viruses expressing envelope glycoproteins variants representative of the quasispecies present in each compartment were generated, and their sensitivity to autologous neutralization, broadly neutralizing antibodies (bNAbs) and entry inhibitors was assessed. Significant compartmentalization of HIV populations between blood and CSF were detected in five out of nine subjects by all tests ($P < 0.01$). Bayesian analyses revealed independent evolution of CSF viral populations for extended periods of time (up to eight years for one patient). There was no difference in sensitivity to autologous neutralization between blood- and CSF-variants, even for subjects with compartmentalization. However, we observed major differences of sensitivity to sCD4 or to at least one bNAb targeting either the N160-V1V2 site, the N332-V3 site or the CD4bs, between blood- and CSF-variants in all cases. Our data show that selective pressure by autologous NAb is not the main driver of HIV evolution in the CNS. Given that each of the conserved neutralizing epitopes is associated to a specific property for cell entry, our data suggest that functional properties of the envelope are responsible for compartmentalization. Considering the possible migration from CSF to blood, the CNS could be a reservoir of bNAb-resistant viruses, an observation that should be considered for immunotherapeutic approaches.

A27 Exploring novel mechanisms of HIV-2 mutagenesis

M. E. Meissner,[1,2,3] S. Baliga,[1] M. Roth,[1] J. Baller,[3,4] and L. M. Mansky[1,2]

[1]Institute for Molecular Virology, Madison, WI, USA, [2]Molecular, Cellular, Developmental Biology, and Genetics Graduate Program, Saint-Paul, MN, USA, [3]Bioinformatics and Computational Biology Graduate Program, Minneapolis, MN, USA, [4]Minnesota Supercomputing Institute, Minneapolis, MN, USA and [5]University of Minnesota, Minneapolis, MN, USA

Over thirty-six million individuals are infected with HIV worldwide. Nearly 95 per cent of these individuals are infected with HIV type 1 (HIV-1), which has a high rate of viral mutation that helps drive immune evasion, disease progression, and rapid emergence of drug resistance. HIV type 2 (HIV-2) accounts for fewer than two million infections overall, remains primarily restricted to West Africa, and exhibits a significantly attenuated disease phenotype compared to HIV-1, characterized by lower rates of transmissibility and a slower progression to AIDS. HIV-2 has recently been found to have a significantly lower rate of mutation compared with HIV-1, which may be related to the differences in viral disease progression and persistence. Although the main driver of HIV mutagenesis is the low fidelity of the virally encoded reverse transcriptase, host factors may contribute to the mutation rate as well. The host protein SAMHD1 has been previously shown to restrict HIV-1 infection in myeloid lineage cells by depletion of dNTP pools through a triphosphohydrolase activity. In addition to inhibiting reverse transcription, this disruption of cellular dNTP levels may contribute to misincorporation of nucleotides and result in mutation of the virus. Here, we propose the use of NGS to explore the role of SAMHD1 on HIV-1 and HIV-2 mutagenesis. Using HIV-1 and HIV-2 Vpx-viruses (which are sensitive to SAMHD1 restriction), we will use