1281. Emergence of a B/F1 HIV Recombinant in the Philippines: A Potentially New Circulating Recombinant Form

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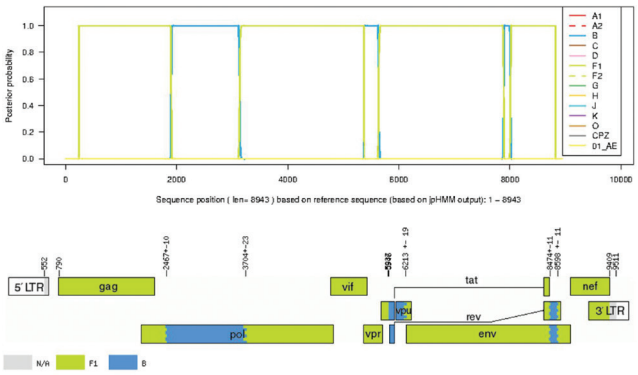
Background. The Philippines has one of the fastest growing HIV epidemics globally. This was accompanied by a switch from subtype B to CRF01_AE. With a large population of returning overseas workers, new subtypes are being introduced regularly. Because diagnosis of HIV in the Philippines is usually late, superinfections can occur and may give rise to new circulating recombinant forms (CRFs). We propose a new CRF from the Philippines.

Methods. Following institutional board approval, treatment-naive patients from two HIV treatment hubs (San Lazaro Hospital and the Philippine General Hospital) were recruited. Blood samples underwent Sanger sequencing of the PR and RT regions and next-generation sequencing (NGS) of near-full length genomes. Sequences were analyzed for recombination using the online tool jumping profile Hidden Markov Model (http://jphmm.gobics.de/).

Results. 247 samples underwent Sanger sequencing of the PR and RT regions of the pol gene. Phylogenetic analysis indicated a clustering of four of the samples. Further analysis showed all four samples had the same breakpoints at nucleotides 2875, 2996, and 3001 (HXB2 numbering). All four patients were male, MSM, with a mean age of 28 years old (24–32), and >10 sexual partners. Mean CD4 count was 464 cells/μL and median viral load was 2.67×10^4 copies/mL. Two patients had sex with foreigners. To get a better overall view of subtype composition, we performed NGS using Illumina HiSeq. NGS showed the majority of the genome to be subtype F1 with segments of subtype B inserted in the pol, vpu, and env genes. A blast analysis of the consensus sequence showed 8,932 out of 8,943 nucleotides (99%) matched a 1999 sample from Argentina. Phylogenetic analysis of these samples show clustering of the four B/F1 recombinants with some South American sequences. No drug resistance mutations were identified.

Conclusion. Mutation and recombination contribute to the extensive genetic diversity of HIV. Understanding this is important in choosing treatment regimens, developing future vaccines, and pursuing epidemiological investigations. The emergence of a new CRF in the Philippines underlies the importance of conducting routine surveillance for new HIV recombinant forms.

Figure 1. New CRF genome showing subtype components.



Disclosures. **All authors:** No reported disclosures.

1282. Detection of HIV Transmitted Drug Resistance by Next-Generation Sequencing in a CRF01_AE Predominant Epidemic

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Background. The Philippines has the fastest growing HIV epidemic in the Asia-Pacific. Concurrent with this is a subtype shift from B to CRF01_AE. We have previously documented transmitted drug resistance (TDR) locally. However, the lack of drug pressure and the insensitivity of Sanger-based sequencing (SBS) may leave archived drug-resistance mutations (DRMs) undetected. To better detect TDR, we performed next-generation sequencing (NGS) on treatment-naïve patients and compared this with SBS.

Methods. Following ethics approval, newly-diagnosed adult Filipino HIV patients were recruited from the Philippine General Hospital HIV treatment hub. Demographic data were collected, and blood samples underwent SBS with a WHO-approved protocol. Whole-genome NGS was performed using Illumina HiSeq through a commercial provider (Macrogen, Korea). Genotype and DRMs were analyzed and scored using the Stanford HIV Drug Resistance Database.

Results. 113 patients were analyzed. Median age was 29 years (range 19–68), mean CD4 count was 147 cells/μL (range 0–556) and median viral load was 2.8×10^6 copies/mL. Genotype distribution was: CRF01_AE (93), B (13), possible CRF01_AE/B recombinants (5), CRF02_AG (1), possible URF (1). TDR prevalence by SBS and NGS at different minority variant cutoffs are shown in Table 1. All DRMs on SBS were found on NGS. Some samples had multiple DRMs. No factors were significantly associated with TDR, genotype, viral load or baseline CD4 count.

Conclusion. NGS is a more sensitive tool for detecting TDR compared with SBS. Nearly double the DRMs were found at an NGS cutoff of ≥5%, including INSTI DRMs. With increasing HIV drug resistance worldwide, switching to NGS may help decrease rates of initial treatment failure, especially in settings with limited repertoires of ARVs.

Table 1. TDR Prevalence by SBS and NGS ($N = 113$).

Method		All (%)	NRTI (%)	NNRTI (%)	PI (%)	INSTI (%)
SBS		11 (9.7)	2 (1.8)	7 (6.2)	3 (2.7)	0 (0)*
NGS	≥1%	59 (52.2)	15 (13.3)	29 (25.7)	19 (16.8)	17 (15.0)
	≥2%	39 (34.5)	7 (6.2)	19 (16.8)	9 (8.0)	10 (8.8)
	≥5%	22 (19.5)	3 (2.7)	15 (13.3)	5 (4.4)	2 (1.8)
	≥10%	19 (16.8)	1 (0.9)	14 (12.4)	4 (3.5)	2 (1.8)
	≥15%	15 (13.3)	1 (0.9)	12 (10.6)	3 (2.7)	1 (0.9)
	≥20%	13 (11.5)	1 (0.9)	10(8.8)	2 (1.8)	1 (0.9)

*SBS for INSTI only done for those with INSTI DRM on NGS ≥ 1% minority variant

Disclosures. **All authors:** No reported disclosures.

1283. Pretreatment HIV-1 Drug Resistance in Transmission Clusters of the Cologne-Bonn Region, Germany

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Background. In Germany, previous reports have demonstrated transmitted HIV-1 drug resistance mutations (DRM) in 10% of newly diagnosed individuals, affecting treatment failure and the choice of antiretroviral therapy (ART). Here, we sought to understand the molecular epidemiology of HIV DRM transmission throughout the Cologne-Bonn region, an area with one of the highest rate of new HIV infections in Europe (13.7 per 100,000 habitants).

Methods. We analyzed 714 HIV-1 ART naïve infected individuals diagnosed at the University Hospitals Cologne and Bonn between 2001 and 2016. Screening for DRM was performed according to the Stanford University Genotypic Resistance Interpretation. Shared DRM were defined as any DRM present in genetically linked individuals (<1.5% genetic distance). Phylogenetic and network analyses were performed to infer putative relationships and shared DRMs.

Results. We detected 123 DRMs in our study population (17.2% of all sequences). Prevalence of any DRM was comparable among risk groups and was highest among people from an endemic area (i.e., country with HIV prevalence >1%) (11/51, 21.6%). Nucleoside-and non-nucleoside reverse transcriptase inhibitor (NRTI/NNNRTI) resistance mutations were detected in 49 (7%) and 97 (13.6%) individuals, with the E138A in 29 (4.1%) and K103N in 11 (1.5%) being the most frequent. Frequency of DRM was comparable in clustering and not clustering individuals (17.1% vs. 17.5%). Transmission network analysis indicated that the frequency of DRM in clustering individuals was the highest in PWID (3/7, 42.9%) (Figure 1A). Genetically linked individuals harboring shared DRMs were more likely to live in suburban areas than in Central Cologne (18.8% vs. 8% of clustering sequences with DRM; Figure 1B).

Conclusion. The rate of DRMs was exceptionally high in the Cologne/Bonn area. Network analysis elucidated frequent cases of shared DRMs among genetically linked individuals, revealing the potential spread of DRMs and the need to prevent onward transmission of DRM in the Cologne-Bonn area.

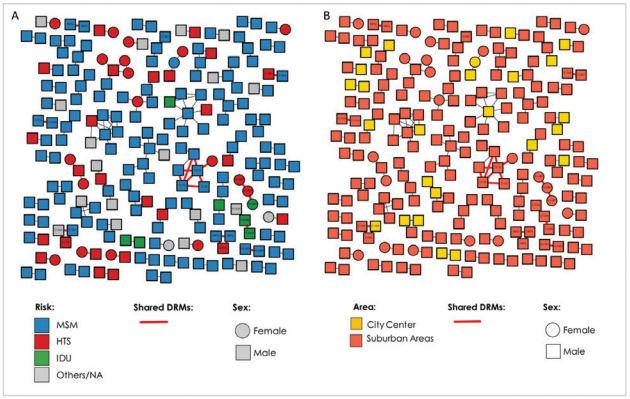

Figure 1. Transmission of pre-treatment drug resistance in the Cologne-Bonn region. A) The color indicates the reported risk group. B) and individuals living in the city center (in orange) or suburban areas (in yellow) of Cologne-Bonn. All edges represent a genetic distance of ≤1.5%. Lines in bold red indicate individuals who shared DRMs. Squares and circles indicating male and female. Only shared DRM are labeled with each nodes. N|NRTIs indicate the presence of ≥1 nucleoside or non-nucleoside reverse transcriptase inhibitor resistance(s).

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1284. Study of Single Nucleotide Polymorphisms Associated with HIV-1 Set-Point Viral Load in Antiretroviral Therapy-Naïve HIV-Positive Participants of the START Study

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Background. HIV-1 set-point viral load (SPVL) is predictive of disease progression and shows variability across HIV-1-positive (HIV+) persons. Various factors may influence SPVL including viral features, environmental exposure and host genetics. To identify single nucleotide polymorphisms (SNPs) associated with SPVL, we performed a genome-wide association study (GWAS) on a subset of participants from the Strategic Timing of AntiRetroviral Treatment (START) study covering a demographically diverse population.

Methods. Consenting participants were antiretroviral therapy (ART)-naïve and SPVL was taken as $\log_{10}$(HIV RNA) at study entry. Genotypic data were generated on a custom content Affymetrix Axiom SNP array covering 770,558 probes. The Ensembl Gene database, assembly GRCh37.p13, was used for annotation. Principal component analysis (PCA) was used to identify population structures, and analysis of variance (ANOVA) was performed to detect associations between SNPs and SPVL. SNPs with zero variance or minor allele frequency (MAF) ≤0.05 were removed.

Results. Among the 2,544 participants, PCA showed distinct population structures with strong separation between black (n = 578) and nonblack (n = 1,966) participants, Figure 1. ANOVA was performed independently on both subsets. Two SNPs located in the Major Histocompatibility Complex (MHC) class I region of chromosome six reached genome-wide significance ($P < 5 \times 10^{-8}$) in the non-black population: rs4418214 ($P = 1.74 \times 10^{-10}$), and rs57989216 ($P = 3.96 \times 10^{-8}$), Figure 2. Two additional SNPs, rs9264942 ($P = 5.99 \times 10^{-8}$) and rs7356880 ($P = 9.69 \times 10^{-8}$), in the same region approached significance. The minor alleles of all four SNPs were associated with lower SPVL, Figure 3. While no SNPs reached genome-wide significance in the black group, we observed similar trends toward lower SPVL for both rs4418214 and rs57989216.

Conclusion. In this study we confirm the association of a previously reported SNP (rs4418214) and identify a novel candidate SNP (rs57989216) associated with lower SPVL in a population of nonblack, ART-naïve HIV+ persons. Current findings suggest that the effects of these SNPs are consistent across race groups, but further studies are required to confirm this. Our results support previous findings that variation in the MHC class I region is a major host determinant of HIV-1 control.

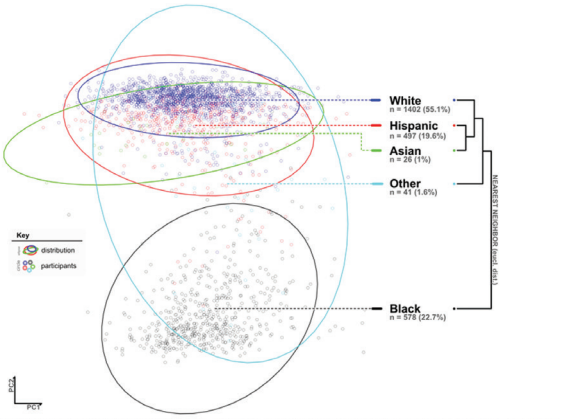

Figure 1. Population structure of the study participants. LEFT: The population structure is illustrated by a principal component analysis (PCA) plot. Each study participant is illustrated by a point that is coloured by race; blue = White, red = Hispanic, green = Asian, black = Black and aqua blue = other. Gaussian estimates are used to visualise the distributions of races in relation to one another (large ellipses). RIGHT: A nearest neighbour dendrogram, calculated on the Euclidean distance between population means, highlights the differences between races.

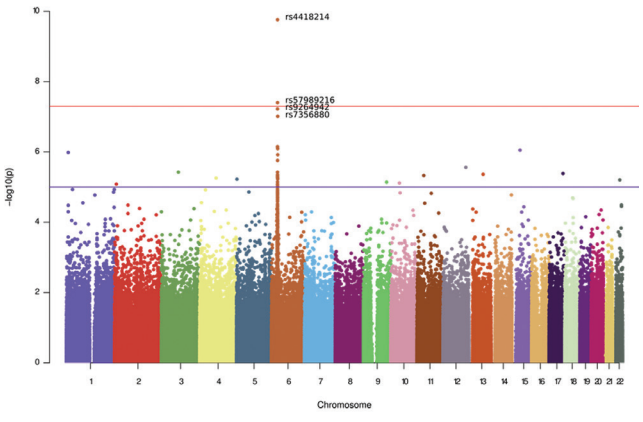

Figure 2. SNPs associated with SPVL in the non-black population. The Manhattan plot shows the association between SNPs and SPVL. Each SNP is represented by a point and plotted by chromosomal location (x-axis), and −log10(*P*) per SNP is shown on the y-axis. Genome-wide significance is indicated by the horizontal red line ($P = 5 \times 10^{-8}$).

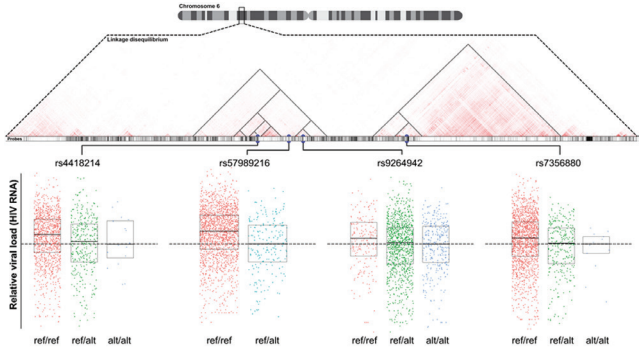

Figure 3. Summary of top four SNPs associated with SPVL. TOP: The location of the four most significant SNPs in the MHC region of chromosome 6. MIDDLE: A heatmap of linkage disequilibrium (LD) highlighting local structures of SNPs in LD with one another. The black line annotations demonstrate the pyramidal, or tree-like, structure of SNP clusters in LD with one another. The positions of the top four SNPs are shown as blue points. The barcode below the heatmap shows the probe coverage of the Affymetrix array in that region, i.e. the SNPs we were able to test for association with SPVL. BOTTOM: Boxplots of SPVL distributions for each of the four SNPs and their different genotypes.

Disclosures. **D. D. Murray**, Centre of Excellence for Health, Immunity and Infectious diseases (CHIP), Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark: Employee, Salary. **J. M. Molina**, Gilead: Scientific Advisor, Consulting fee. Merck: Scientific Advisor, Consulting fee. ViiV: Scientific Advisor, Consulting fee. Teva: Scientific Advisor, Consulting fee.

1285. Impact of an Educational Program on Knowledge, Attitude and Practice to Prevent HIV Infection Among HIV-Negative Heterosexual Partners of HIV-Infected Patients

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