

resistance-associated substitutions (RAS) is an important contributor to this decision-making process. In the present study in an Irish cohort, we performed a retrospective analysis on all HCV samples received for drug resistance testing at the Irish National Virus Reference Laboratory between September 2014 and May 2016. Particular attention was paid to patients who experienced virological failure in an attempt to identify predictors of failure. Sanger sequence data covering the HCV NS3 protease coding region were obtained for 682 samples received during the study period. These were analysed using PAUP phylogenetic software. Sequence data for the NS5A and NS5B regions in some samples were also obtained. The rs12989860 single nucleotide polymorphism site was examined by allelic discrimination real-time PCR. Analysis of the NS3 viral sequences demonstrated that 85.5% (583/682) were HCV subtype 1a, 14.2% (97/682) subtype 1b and 0.3% (2/682) subtype 1c infections, subtype 1a was further differentiated into 76% clade 1 (443/583) and 24% clade 2 (140/583). RAS proven to reduce susceptibility to NS3 inhibitor treatment were detected in 45.9% of cases (313/682). Although the vast majority of all RAS detected were found in subtype 1a viruses, 7.2% (7/97) subtype 1b samples also contained one or more RAS. The Q80K polymorphism was found in 313/583 (57.3%) of HCV subtype 1a, and almost exclusively in clade 1 (242/443; 54.6%) versus clade 2 viruses (2/140; 1.4%). This distribution is reflected in the neighbour joining tree. Among the cohort of patients who experienced virological failure whilst on treatment, RAS could be detected in 11/17 (64.7%) patients for whom sequence could be generated. These included V36M/L (6/11; 54.5%), Q80K (5/11; 45.5%), R155K/T (3/11; 27.3%) and T54S (1/11; 9.1%). The majority of these patients were found to possess the deleterious “T” single nucleotide polymorphism (SNP) at the rs12989860 site within the Interferon lambda 4 (INF λ 4) gene locus. Nine of eleven patients with detected RAS were found to also be either CT or TT at rs12989860, one patient was CC at this SNP. Preliminary data from patients experiencing treatment failure on NS5A/B inhibitors also indicate the presence of RAS in 4 of 7 individuals. The high incidence of RAS within HCV NS3 protease sequences, the detection of RAS in NS5A sequences, and the apparent risk of treatment failure, albeit in a small number of patients, when the RAS are present, highlights the importance of sequencing these viruses prior to commencing treatment with protease inhibitors, and the need to identify additional predictors of failure.

A13 HIV drug resistance over a decade of antiretroviral therapy scale-up for HIV/AIDS patients in Vietnam

L.A. Nguyen,¹ D.H. Do,¹ L.T. Nguyen,^{1*} N.T. Do,² H.H. Nguyen,² V.T. Nguyen,³ D.Q. Vu,⁴ H.T. Nguyen,¹ M. Kato,⁵ M.R. Jordan,⁵ D.D. Bui,²

¹National Institute of Hygiene and Epidemiology, Vietnam, ²Vietnam Authority for HIV AIDS Control, ³World Health Organization, Vietnam, ⁴Hanoi Medical University, Vietnam and ⁵Tufts University School of Medicine, Massachusetts, USA

Since 2005, Vietnam has remarkably scaled-up Antiretroviral therapy (ART) for HIV-infected people. The number of people receiving ART has increased from 2,670 in 2005 to 78,438 adults and 4,204 children at the end of 2013. ART coverage increased to 67% (60.0% in adults and 78.1% in children), against current eligibility criteria per National Guideline (CD4 cells <350 cells/ml). Standardized ART was delivered at 364 outpatient clinics at the end of 2013. Since 2010, the Ministry of Health has recommended the first-line prioritized ART regimens with two NRTIs (d4T + 3TC or ZDV + 3TC) plus one NNRTI (nevirapine [NVP]). In

the context of rapid ART scale-up, the extent of HIV drug resistance (HIVDR) in Vietnam has been concerned, studies on transmission and emergence of HIV drug resistance were carried out in 2013–4. HIVDR study protocols were adapted from WHO guidelines for transmitted drug resistance (TDR) (2012) and acquired drug resistance (ADR) (2014). In brief, the TDR survey was implemented in a total of 15 voluntary counseling and testing (VCT) sites located in the old Hanoi. A total of 74 eligible VCT clients, aged 18–24, detected HIV positive, had no history of ART exposure, had no previous pregnancy if female, and were sequentially sampled. HIV genotyping was done in order of enrollment date until DR prevalence could be classified. For the ADR survey, 8 ART outpatient clinics were sampled from a total of 114 clinics that had ART available for more than 3 years up to the end of 2010, in the North, using probability proportional to proxy size (PPPS) sampling method. From each selected VCT, 23 patients who had received ART for more than 36 months were consecutively recruited into the study. All patients were taken blood for evaluating viral suppression and HIV drug resistance if viral load above 1,000 copies/ml. The prevalence of transmitted HIV drug resistance was classified as moderate between 5 and 15%, mainly to NRTIs/NNRTIs, no protease inhibitor (PI) resistance. In 181 patients on ART for more than 36 months, 93.9% (95% CI: 90.4–97.4%) had viral load suppression and 5.5% (95% CI: 2.2–8.9%) had drug resistance. Notably, 100% of individuals with viral suppression failure are resistant to all drugs in both their initial and current ART regimes receiving. Against 7 NRTIs and 4 NNRTIs recommended for the first-line ART as per the national guideline, resistance rates ranged between 75 and 100%. No resistance to PIs was found. The most common mutations are M184V (90%), D67G (60%), K70RES (60%), K103N (50%), Y184C (50%), T215FYN (50%), and K219QE (50%). The scaled-up ART program in Vietnam was proven to be effective with high rate of viral suppression at 36 months on the first-line prioritized ART regimens. Transmitted HIV DR to NRTIs/NNRTIs was increased, requiring the national program on HIV DR surveillance and prevention be strengthened to maximize long-term effectiveness of first-line ART regimens.

A14 Comprehensive characterisation and evolutionary analysis of endogenous retroviruses in the mouse genome

Tristan P.W. Dennis, Henan Zhu, Sam J. Wilson, and Robert J. Gifford

MRC-University of Glasgow Centre for Virus Research, Glasgow, UK

It is well established that the genome of the mouse (*Mus musculus musculus*) contains large numbers of transposable elements, including many endogenous retroviruses (ERVs). Murine ERV lineages have been characterized piecemeal, but a comprehensive analysis has yet to be implemented. In this study, we address this by combining high-throughput *in silico* screening of the mouse genome with in-depth phylogenetic analysis of murine ERVs. Based on phylogenetic analysis of ERV polymerases, we establish the presence of at least 22 major ERV lineages in the murine genome, of which only 14 have been previously described. The majority of the previously unreported lineages are relatively low copy number (<100). Using a combination of automated and manual approaches we were able to recover representative internal regions and long terminal repeats (LTRs) for four of the eight novel lineages. LTR sequences were used to infer calibrated timelines of ERV invasion and intragenomic expansion within the mouse genome. These data were transposed against a timeline of murine evolution and phylogeography, providing new insights into the coevolutionary