

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,900

Open access books available

124,000

International authors and editors

140M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



# HIV-1 Diversity and Its Implications in Diagnosis, Transmission, Disease Progression, and Antiretroviral Therapy

Inês Bártole and Nuno Taveira  
*Centro de Investigação Interdisciplinar Egas Moniz (CiiEM),  
Instituto Superior de Ciências da Saúde Egas Moniz,  
Monte de Caparica and Unidade dos Retrovírus e Infecções Associadas,  
Centro de Patogénese Molecular,  
Faculdade de Farmácia de Lisboa,  
Portugal*

## 1. Introduction

Due to an error prone reverse transcriptase, HIV-1 has diversified into multiple variants. Currently, there are four phylogenetic groups named M, N, O and P (Gurtler et al., 1994; Plantier et al., 2009b; Simon et al., 1998). HIV-1 group M, which is responsible for most of the infections in the world, has diversified into nine subtypes named A, B, C, D, F, G, H, J and K, seven sub-subtypes (A1-A5 and F1-F2), multiple circulating recombinant forms (CRFs) and countless unique recombinant forms (URFs) (Gao et al., 2001; Meloni et al., 2004; Triques et al., 1999; Vidal et al., 2009; Vidal et al., 2006). At present, 49 CRFs were recognized of which 37 are first generation recombinants and 12 are second generation recombinants (Los Alamos Sequence Database, 2011).

Five HIV-1 strains dominate the global epidemic: subtypes A, B, and C, along with CRF01\_AE and CRF02\_AG, with subtype C accounting for almost 50% of all HIV-1 infections worldwide (Buonaguro, Tornesello, and Buonaguro, 2007; McCutchan, 2006; Santos and Soares, 2010; Taylor and Hammer, 2008). Molecular epidemiological studies show that, with the exception of sub-Saharan Africa where almost all subtypes, CRFs and several URFs have been detected there is a specific geographic distribution pattern for HIV-1 subtypes (Buonaguro, Tornesello, and Buonaguro, 2007; McCutchan, 2006; Santos and Soares, 2010; Taylor and Hammer, 2008). Subtype A is prevalent in Central and Eastern Africa (Kenya, Uganda, Tanzania, and Rwanda) (Harris et al., 2002; Morison et al., 2001; Songok et al., 2004), Iran (Tagliamonte et al., 2007), Eastern Europe (Bobkov et al., 1997; Bobkov et al., 2004), and Central Asia (Beyrer et al., 2009; Eyzaguirre et al., 2007). Subtype B predominates in developed countries, such as United States of America (USA) and Canada (Akouamba et al., 2005; Brennan et al., 2010; Carr et al., 2010a; Jayaraman et al., 2003), in Brazil (Dumans et al., 2004; Monteiro-Cunha et al., 2011; Santos et al., 2006), countries of Western and Central Europe (Abecasis et al., 2011; Castro et al., 2010; De Mendoza et al., 2009; Easterbrook et al., 2010; Galimand et al., 2010; Habekova et al., 2010; Kousiappa, Van

De Vijver, and Kostrikis, 2009; Lai et al., 2010; Parczewski et al., 2010) and Australia (Herring et al., 2003; Ryan et al., 2004), and is also common in several countries of Southeast Asia (Chen et al., 2010; Lau et al., 2010), northern Africa (Annaz et al.) and the Middle East (Sarrami-Forooshani et al., 2006). Subtype C is the overwhelming prevailing strain in Southern Africa (Bartolo et al., 2009b; Gonzalez et al., 2010; Lahuerta et al., 2008; Papathanasopoulos et al., 2010), in India and neighbor countries (Neogi et al., 2009a; Neogi et al., 2009b) and in the southern region of Brazil (Monteiro-Cunha et al., 2011). Subtype D strains are found mainly in East Africa, and to a lesser extent in West Africa (Conroy et al., 2010; Harris et al., 2002; Laukkanen et al., 2000; Songok et al., 2004). Subtype F predominates in Central Africa (Carr et al., 2010b; Soares et al., 2010), South America (Avila et al., 2002; Munerato et al., 2010) and Eastern Europe (Fernandez-Garcia et al., 2009; Paraschiv, Foley, and Otelea, 2011). Subtype G viruses are prevalent in Central and Western Africa (Hawkins et al., 2009; Kalish et al., 2004), as well as in Portugal (Abecasis et al., 2011; Esteves et al., 2003; Esteves et al., 2002; Palma et al., 2007) and Spain (De Mendoza et al., 2009; Trevino et al., 2011). Subtypes H and J were described in Central Africa (Janssens et al., 2000; Mokili et al., 1999; Yamaguchi et al., 2010) and in Angola (Bartolo et al., 2005; Bartolo et al., 2009d). Subtype K was identified in DRC and Cameroon (Triques et al., 2000).

Some CRFs have high impact in local AIDS epidemics, such as CRF01\_AE in Southeast Asia (Gao et al., 1996; Magiorkinis et al., 2002) and CRF02\_AG in Western and Central Africa (Cornelissen et al., 2000; Fischetti et al., 2004a; Fischetti et al., 2004b). CRF11\_cpx was the first second generation CRF described in 2000 in patients from Cameroon (Tscherning-Casper et al., 2000). This CRF circulates in Cameroon, Central African Republic, Gabon, DRC, and Angola although its exact prevalence rate remains to be determined ( Djoko et al., 2011). Second generation CRFs are becoming common in complex epidemics with multiple subtypes and recombinant forms. At present they have been detected in Africa, East Asia, Thailand, Malaysia, Estonia and Saudi Arabia (Djoko et al., 2011).

HIV-1 group O seems to be endemic in Cameroon and neighboring countries in West-Central Africa and represents only about 1-5% of HIV-1 positive samples in this region (Peeters et al., 1997; Yamaguchi et al., 2004). Elsewhere in the world, group O viruses have been identified mainly from people with epidemiological links to the referred Central African countries (Lemey et al., 2004). HIV-1 groups N and P circulate exclusively in Cameroon (Brennan et al., 2008; Plantier et al., 2009b; Vallari et al., 2010; Vallari et al., 2011). In some regions of the world, little information is available about HIV diversity, particularly in North Africa, the Middle East, and parts of Central Asia.

Differential characteristics of viral subtypes and their interactions with the human host may influence HIV transmission and disease progression. HIV-1 genetic diversity may also impact the susceptibility and resistance to antiretroviral drug as well as the performance of diagnostic and viral load assays. The aim of this Chapter was to review the current knowledge on HIV-1 diversity and its implications in diagnosis, transmission, disease progression, and antiretroviral therapy and resistance.

## **2. Impact of HIV-1 diversity in transmission**

Although earlier studies found an association between CRF01\_AE and heterosexual transmission and between subtype B and intravenous drug use (Gao et al., 1996; Soto-

Ramirez et al., 1996), a more recent longitudinal study performed in Thailand found an increased probability of CRF01\_AE transmission among IDUs compared with subtype B (Hudgens et al., 2002). A recent study performed in HIV-discordant couples in Uganda found that subtype A was associated with a significant higher rate of heterosexual transmission than subtype D ( $P=0.01$ ) (Kiwauka et al., 2009). The rate of transmission may reflect differences in subtype-specific coreceptor tropism. HIV-1 can use as coreceptors CCR5 (R5 variants), CXCR4 (X4 variants) or both (R5X4 variants or dual tropic) to enter the cells (Schuitemaker, van 't Wout, and Lusso, 2011). R5 variants are largely prevalent during primary infection and seem to be more easily transmitted or established in the newly infected host than X4 strains (Schuitemaker, van 't Wout, and Lusso, 2011). An increased prevalence of X4 variants has been reported for subtype D which may in part explain their reduced heterosexual transmissibility when compared to other genetic forms (Huang et al., 2007; Kaleebu et al., 2007; Kiwauka et al., 2009; Tscherning et al., 1998).

Several studies have looked for variations between clades in mother-to-child HIV-1 transmission (MTCT) rates. In Kenya, MTCT appeared to be more common among mothers infected with subtype D compared with subtype A ( $P=0.002$ ) and this association was independent of other risk factors for MTCT, such as maternal HIV viral load, episiotomy or perineal tear, and low birth weight (Yang et al., 2003). On the other hand, in Tanzania HIV-1 subtypes A (odds ratio, 3.8; 95% CI, 0.8-24.7%) and C (odds ratio, 5.1; 95% CI, 1.3-30.8%) were more frequently transmitted from mother-to-child than subtype D (Renjifo et al., 2001). In another study, the risk of MTCT was higher in women infected with subtype C, followed by subtype A, and was lowest in women infected with subtype D (John-Stewart et al., 2005). It was found that pregnant women, infected with subtype C were more likely than those infected with subtype A or D ( $P=0.006$ ) to shed HIV-1-infected vaginal cells even after adjusting for age, CD4 cell count, and plasma HIV-1 viral load. Another study in Tanzania presented similar results, with preferential in-utero transmission of HIV-1 subtype C compared to HIV-1 subtype A or D ( $P=0.026$ ) (Renjifo et al., 2004). Other researchers, however, found no association between subtype and rates of MTCT (Martinez et al., 2006; Murray et al., 2000; Tapia et al., 2003). Moreover, in studies where pregnant women received a single-dose nevirapine (sdNVP) prophylaxis no significant differences were observed in the rate of MTCT in women infected with HIV-1 subtype A, D or C (Eshleman et al., 2006; Eshleman et al., 2005a).

Many factors, such as maternal stage of the disease, maternal immunological status, viral load, mode of delivery, duration of breast-feeding, ARV prophylaxis, maternal plasma vitamin A (associated with AIDS progression), and close maternal-child Human Leukocyte Antigen (HLA) matching, can contribute to these differences (Fowler and Rogers, 1996; MacDonald et al., 1998; McGowan and Shah, 2000). Nevertheless, the role of viral determinants in MTCT has yet to be well established (Dickover et al., 2001). Several studies have shown that viral diversity in the mother is generally higher than that present in the infant, suggesting that maternal viruses are selected before transmission (Ahmad, 2005; Zhang et al., 2010b). Several factors like specific viral selection (Wolinsky et al., 1992), neutralization resistance (Dickover et al., 2006; Wu et al., 2006; Zhang et al., 2010a) and enhanced replicative capacity of the transmitted viruses (Kong et al., 2008) have been

associated with a bottleneck type transmission. The basis for the MTCT bottleneck is an issue that needs further clarification.

In summary, it remains to be determined whether there is a true association between subtypes and adult or MTCT transmission of HIV-1 or whether the differences in transmission probabilities found in some studies are associated with several other factors that can influence HIV transmission, e.g. behavioral, epidemiological and immunological (Attia et al., 2009). More longitudinal and well controlled studies, preferentially performed in a single area and with a single ethnic group of HIV-1 infected patients, are needed to identify HIV-1 determinants for adult and vertical transmission and to evaluate the potential association of subtype with transmission.

### 3. Impact of HIV-1 diversity in disease progression

Another important question is whether clade differences result in variable rates of disease progression. There have been several prospective, observational studies of the course of HIV-related disease in cohorts infected with various HIV-1 genetic forms. Although some studies did not find an association between HIV-1 clades and disease progression (Alaeus et al., 1999; Amornkul et al., 1999; Galai et al., 1997; Laurent et al., 2002; Taylor and Hammer, 2008), more recent studies established this association (Easterbrook et al., 2010; Keller et al., 2009; Kiwanuka et al., 2010). A retrospective cohort study (1996-2007) reported that Africans patients infected with HIV-1 non-B subtypes (A, C, F-K, AC, AE, AG, BF and DF) had slower rates of disease progression compared to Haitians ( $P=0.0001$ ) and Canadians ( $P=0.02$ ) infected with subtype B viruses (Keller et al., 2009).

Earlier studies found that subtype D was associated with the most rapid disease progression relative to other subtypes (Taylor and Hammer, 2008). A very recent study in patients from Rakai, Uganda, reported that infection with subtype D is associated with significantly faster rates of CD4 T-cell loss than subtype A ( $P<0.001$ ), which might explain the more rapid disease progression for subtype D compared with subtype A (Kiwanuka et al., 2010). Along the same lines, a study conducted in 2010 in an ethnically diverse population of HIV-1-infected patients in South London showed a faster CD4 cell decline and higher rate of subsequent virological failure with subtype D infection than with subtypes B ( $P=0.02$ ), A ( $P=0.004$ ) or C ( $P=0.01$ ) (Easterbrook et al., 2010).

An important unanswered question is the biological basis for these differences. A possible clue comes from data suggesting that emergence of X4 variants, which in subtype B are associated with increased CD4 depletion and disease progression [302-304], was more common in HIV-1 subtype D compared with subtype A ( $P=0.040$ ) (Kaleebu et al., 2007; Tscherning et al., 1998). Other study found that subtype D may be dual tropic more frequently than the other subtypes (Huang et al., 2007). The earlier switch to X4 usage in subtype D isolates may explain the faster rate of CD4 decline and disease progression with this subtype (Kaleebu et al., 2007; Tscherning et al., 1998).

One study reported the presence of X4 or R5X4 isolates at early stages of infection, in addition to a decrease in CD4+ counts, in all patients infected with CRF14\_BG (Perez-Alvarez et al., 2006). We have shown recently that most CRF14\_BG strains (78.9%)

sequenced to date use CXCR4 (Bártolo et al., 2011) and that patients infected with this CRF can progress very quickly to AIDS and death (Bartolo et al., 2009a). Together, these results suggest that, like HIV-1 subtype D, CRF14\_BG may be highly pathogenic (Kuritzkes, 2008; Sacktor et al., 2009). The rapid disease progression associated with CRF14\_BG may be due to an earlier switch to X4 phenotype driven by the selective pressure of neutralizing antibodies (Bártolo et al., 2011). However, the relationship between higher tendency for X4 use and higher disease progression may not hold for other subtypes. For instance, the percentage of X4 virus appears to be lower in subtype C than in subtype B, even when the viruses are obtained from patients with AIDS (Casper et al., 2002; Cilliers et al., 2003; Ping et al., 1999).

It is important to note that most of these studies of disease progression have confounder factors such as access to medical care, nutritional status, host genetic factors, and mode of viral transmission, which may contribute to the divergent results (Pereyra et al., 2010). More studies are needed to confirm previous conflicting results, and to elucidate the host-viral interactions that may lead to more favorable outcomes in individuals infected with various genetic forms of HIV-1. This kind of studies should be longitudinal, performed with a higher number of patients, preferentially in primary infection, in a single country to better control ethnic and genetic factors of the patients, and with several genetic forms of HIV-1.

#### **4. Impact of HIV-1 diversity in diagnosis and disease management**

Acute infection with HIV-1 can be identified and quantified using several virological and immunological markers (Figure 1) (Fiebig et al., 2003). In the first eleven days after infection viral markers are undetectable in the blood (window period). Plasma HIV RNA levels begin to increase at the 10<sup>th</sup> day, peaking around 20 days after infection. HIV p24 levels typically peak around 20 days after infection. Antibody response starts to be detectable by ELISA assays after 20 days of infection, on average. Serological and molecular assays have been designed to detect and/or quantify one or more of these HIV infection markers. These assays should be able to detect all genetic forms of HIV but the very high genetic and antigenic evolution of this virus along with the continued diversification and global redistribution of HIV groups, subtypes and recombinants may affect their performance.

##### **4.1 Immunoassays**

HIV fourth-generation assays detect both HIV antibodies and the p24 antigen. These assays provide an advantage for detection of infection during the window period prior to seroconversion since the diagnostic window may be reduced by an average of 5 days relative to an IgM-sensitive EIA (Fiebig et al., 2003; Weber et al., 1998). However, some fourth-generation assays showed low sensitivity in the detection of p24 antigen from some non-subtype B HIV-1 strains (A, C, F, H, CRF01\_AE, O) (Kwon et al., 2006; Ly et al., 2007; Ly et al., 2004; Ly et al., 2001; Weber, 2002). This low sensitivity in antigen detection may be attributed to differences in viral epitopes of the different HIV genetic forms which may not be recognized by the monoclonal antibody used in the assay (Plantier et al., 2009a).

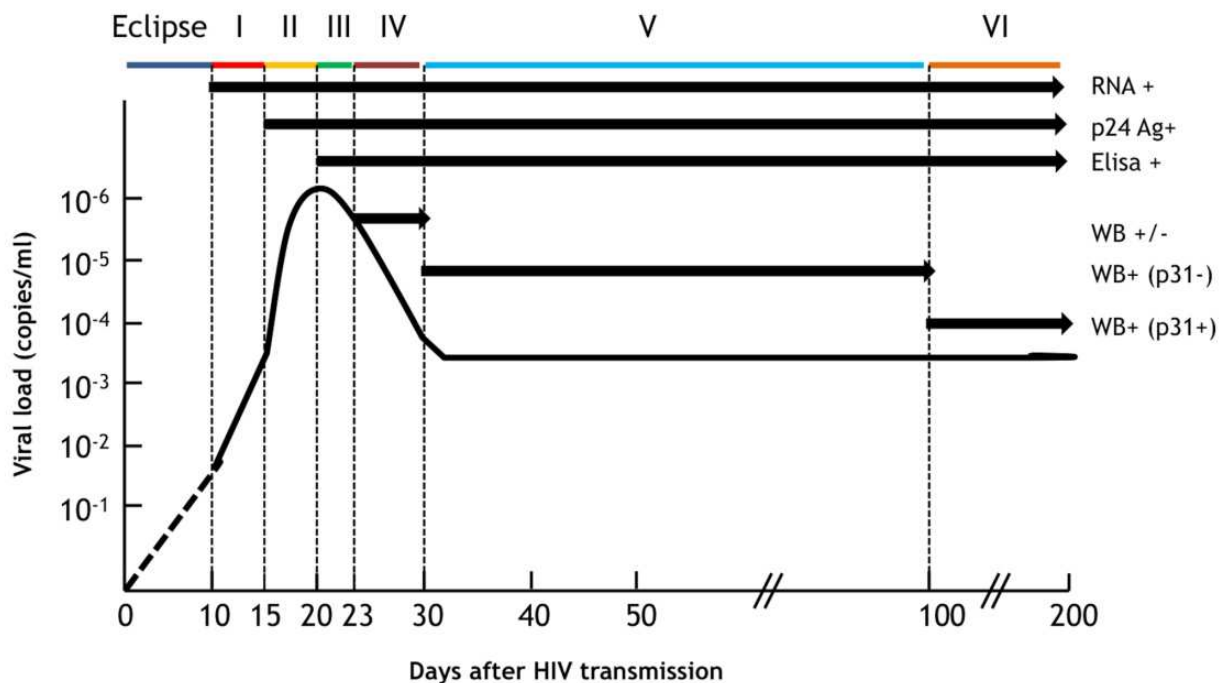


Fig. 1. Progression of HIV-1 markers in acute infection. WB, Western blot; RNA, HIV RNA; LS-Ab, HIV antibody determined by sensitive/less sensitive enzyme immunoassay testing strategy; p24 Ag, HIV p24 antigen, from time of exposure (day 0) through the first 200 days of infection. Eclipse, eclipse period (undetectable viral markers in blood samples); Stage I (definitive HIV RNA viremia), stage II (p24 antigenemia), stage III (HIV EIA antibody reactive), stage IV (I, Western blot indeterminate), stage V (Western blot positive without p31 pol band) and stage VI (P, Western blot positive with p31 pol band). Adapted from (Fiebig et al., 2003).

The major target for HIV-1 antibodies in immunoassays is the *env* gp41 immunodominant region (IDR). Key epitope(s) targeted by these assays might be modified or eliminated by the occurrence of natural polymorphisms within the IDR region associated with the genetic variation of HIV-1, ultimately leading to reduced sensitivity or lack of antibody detection (Brennan et al., 2006; Gaudy et al., 2004). A few cases of false-negative results involving, for example, subtypes B, C, and F, and resulting from major mutations of the IDR epitope have been described (Aghokeng et al., 2009; Gaudy et al., 2004; Ly et al., 2007; Ly et al., 2004; Ly et al., 2001; Zouhair et al., 2006).

Earlier analysis of specimens from patients infected with group O viruses revealed that some commercial immunoassays failed to detect group O infections (Eberle et al., 1997; Loussert-Ajaka et al., 1994; Schable et al., 1994; Simon et al., 1994). This ultimately led to incorporation of group O specific antigens and/or peptides into the assays to improve detection of group O infections (van Binsbergen et al., 1996). Nonetheless, false-negative results continue to be reported for some patients infected with HIV-1 group O (Henquell et al., 2008; Plantier et al., 2009a; Zouhair et al., 2006).

Despite the high genetic divergence between HIV-1 groups M and N, all group N infections studied until now were detected by five commercial HIV immunoassays (Vallari et al., 2010). Group P infections may not be efficiently detected by the current HIV screening tests due to the absence of group P-specific reagents for antibody detection (Vallari et al., 2011). Nevertheless, Plantier et al., in the first report regarding detection of group P infections, found that several HIV-1 screening tests were reactive against this group (Plantier et al., 2009b). Despite the absence of either HIV-1 group N or group P specific antigens in most assays, antibodies targeting some group M specific antigens may cross-react with group N and P antigens allowing for the serologic detection of infections by HIV-1 isolates from these groups.

Serological diagnosis of HIV-1 infection in Sub-Saharan Africa is mostly done with rapid tests (Plate, 2007). This kind of assay is simple, rapid, instrument-free and relatively cheap. However some of these assays have shown problems in detecting HIV-1 subtypes D, F, H, CRF02\_AG, group O and HIV-2 (Aghokeng et al., 2009; Beelaert and Fransen, 2010; Chaillet et al., 2010; Holguin et al., 2009; Laforgerie et al., 2010; Pavie et al., 2010). Minor antigenic differences between isolates of different clades and the peptides/recombinant proteins used in these assays could explain the problems in the detection of some HIV genetic forms (Aghokeng et al., 2009; Laforgerie et al., 2010; Makuwa et al., 2002; Pavie et al., 2010). Low sensitivity of some of these tests can also be associated with low level of HIV-specific antibodies due to recent seroconversion, early and stringent control of viral replication by antiretroviral therapy, or immune exhaustion in end-stage AIDS patients (Apetrei et al., 1996; Ferreira Junior et al., 2005; Jurriaans et al., 2004; Laforgerie et al., 2010; Makuwa et al., 2002; Pavie et al., 2010; Spivak et al., 2010).

#### 4.2 Viral load assays

A variety of nucleic acid based diagnostic assays that quantify plasma HIV-1 RNA levels have been developed and used to monitor disease progression and response to antiviral therapy, detect primary infection [plasma HIV RNA levels begin to be detectable about 11 days after infection (Figure 1)], detect HIV infection among perinatally exposed infants and HIV vaccine recipients, and detect HIV infection in the absence of antibodies (Table 1)(Bill & Melinda Gates Foundation, 2009; European AIDS Clinical Society, 2009; Korenromp et al., 2009; Mellors et al., 1997; Thompson et al., 2010). These assays rely on HIV-1 sequence-specific primers and/or probes and use technologies such as reverse transcriptase polymerase chain reaction (RT-PCR) amplification, isothermal nucleic acid sequence-based amplification (NASBA), branched-chain DNA signal amplification (bDNA) and real-time (RT) PCR (Collins et al., 1997; de Mendoza et al., 2005; Dyer et al., 1999; Johanson et al., 2001; Rouet et al., 2005; Stevens et al., 2005; Sun et al., 1998; Yao et al., 2005). The genetic variation of HIV-1 presents challenges to the design of quantitative assays that measure HIV-1 RNA or DNA levels. Reliable quantification can be compromised by natural polymorphisms occurring in primer/probe sequences that have the potential to reduce or abolish hybridization (Christopherson, Sninsky, and Kwok, 1997; Kwok et al., 1990). Genetically divergent variants may go unrecognized since, usually, subtype and target sequence information is not known at the time of testing.

Several comparative studies have shown that the sensitivity and specificity of viral load assays varies depending on HIV-1 group or subtype, especially in non-B subtypes, complex recombinant forms and groups O, N, and P viruses (Bourlet et al., 2011; Church et al., 2011;



Assays	Technology	Probe target	Linear range (RNA copies/ml)	HIV-1 clade recognition
Abbot Real Time HIV-1	RT-PCR	<i>pol</i> -INT	40-10,000,000	Group M (subtypes A-H), several CRFs and Groups O and N
Amplicor HIV-1 Monitor Test v1.5	RT-PCR	<i>gag</i> -p24	Standard protocol: 400 to >750,000; Ultra-sensitive: 50 - >100,000	HIV-1 Group M (subtypes A-H)
Cobas Amplicor HIV-1 Monitor Test, v1.5	RT-PCR	<i>gag</i>	Standard protocol: 400 to >750,000; Ultrasensitive: 50 - >100,000	HIV-1 Group M (subtypes A-H)
Cobas AmpliPrep/Cobas TaqMan HIV-1 Test, v2.0	RT-PCR	<i>gag</i> -p41 and 5'LTR	20-10,000,000	Group M, several CRFs, and Group O
Versant HIV-1 RNA 1.0 Assay (kPCR)	RT-PCR	<i>gag</i> -p24	37-11,000,000	HIV-1 Groups M and O
Versant HIV-1 RNA 3.0 Assay	bDNA	<i>pol</i> -INT	50-500,000	HIV-1 Group M
NucliSens EasyQ HIV-1 v2.0	NASBA	<i>gag</i> -p24	10- 10,000,000	HIV-1 Group M (subtypes A-J), CRF01_AE, and CRF02_AG

Adapted from (World Health Organization, June 2010).

Table 1. Viral load assays approved by FDA and recommended by WHO

Geelen et al., 2003; Gottesman et al., 2006; Holguin et al., 2008; Katsoulidou et al., 2011; Plantier et al., 2009b; Rouet et al., 2010; Scott et al., 2009; Swanson et al., 2005; Swanson et al., 2006; Swanson et al., 2007; Tang et al., 2007; Wirden et al., 2009; Xu et al., 2008). However, the newer quantitative real-time PCR (qRT-PCR) methods (i.e., m2000rt Abbot Real Time HIV-1 Assay or Cobas AmpliPrep/COBAS TaqMan) showed a higher performance on HIV viral load testing of patients with subtype B as well as patients with non-B subtype infections (Bourlet et al., 2011; Church et al., 2011; Katsoulidou et al., 2011; Swanson et al., 2007; Tang et al., 2007). Abbot Real Time HIV-1 Assay seems to be the only assay prepared to detect all HIV-1 subtypes, several CRFs, as well as group N, and O viruses (Church et al., 2011; Swanson et al., 2007; Tang et al., 2007). This is probably related with the high level of genetic conservation of the integrase gene that this test amplifies (Young et al., 2011). In contrast, bDNA (Versant v3.0) and NASBA (EasyQ) assays are considerably less reliable for accurate viral load measurements across HIV clades (Bourlet et al., 2011; Church et al., 2011; Katsoulidou et al., 2011; Swanson et al., 2007; Tang et al., 2007). In summary, available data indicates that HIV-1 assays targeting the highly conserved *pol* integrase region of the HIV-1 genome may be subject to less variability than assays targeting the *gag* gene (Geelen et al.,

2003; Swanson et al., 2005; Swanson et al., 2006; Swanson et al., 2007). As HIV genetic diversity evolves, evaluations of all commercially licensed HIV-1 viral load assays should be performed regularly in populations with patients infected with all viral subtypes.

Failed detection or unreliable quantification of HIV infection can have significant consequences in early detection of MTCT (Creek et al., 2007; Geelen et al., 2003). Early diagnosis in infants can only be achieved with tests that detect HIV-1 DNA or RNA, since maternal HIV antibodies can persist in the infant until month 18 (Read, 2007) thereby precluding the use of antibody detection tests. It has been recommended that diagnostic testing with HIV-1 DNA or RNA assays be performed within the first 14-21 days of life, at 1-2 months and at 4-6 months of age (AIDSinfo, May 24, 2010). Additionally, if any of these test results are positive, repeat testing on a second sample has to be done to confirm the diagnosis of HIV-1 infection. A diagnosis of HIV-1 infection can be made on the basis of 2 separate positive HIV-1 DNA or RNA assay results (New York State Department of Health AIDS Institute, 2010).

Viral load assay	Extraction method	Lower detection limit (log <sub>10</sub> HIV-1 RNA copies/ml)	Reference
COBAS TaqMan RT-PCR Assay	Nuclisens MiniMAG	3.0 (96.4% detected)	(Andreotti et al., 2010)
COBAS TaqMan RT-PCR Assay	Primagen	3.0 (96 % detected)	(Waters et al., 2007)
Nuclisens EasyQ HIV-1 v2.0	Nuclisens EasyMAG	2.9 (95% detected)	(van Deursen et al., 2010)
Nuclisens EasyQ HIV-1 v2.0	Manual Nuclisens	3.5 (100% detected)	(Johannessen et al., 2009)
Nuclisens EasyQ HIV-1	Nuclisens MiniMAG	2.9 (100% detected)	(Kane et al., 2008)
Amplicor HIV-1 Monitor Test v1.5	In-house method	3.0 (100% detected)	(Ikomey et al., 2009)
Abbot Real Time HIV-1	m2000 RT system	3.7 (100% detected)	(Garrido et al., 2009)
Abbot Real Time HIV-1	m2000 RT system	2.6 (99% detected)	(Lofgren et al., 2009)
Abbot Real Time HIV-1	m2000 RT system	3.0 (100% detected)	(Mbida et al., 2009)

Adapted from (Johannessen, 2010).

Table 2. Recent studies comparing HIV-1 viral load assays in DBS and plasma

Amplicor HIV-1 DNA PCR test version 1.0 (Roche Diagnostic), the first commercial HIV-1 qualitative DNA PCR assay, lacked optimal sensitivity to detect non-B HIV-1 subtypes (Bogh et al., 2001; Kline, Schwarzwald, and Kline, 2002; Obaro et al., 2005). In May 2005,

Roche Diagnostics replaced Amplicor HIV-1 DNA PCR version 1.0 by version 1.5, which has been shown to have excellent sensitivity and specificity in testing adult venous blood samples and infant DBS (Germer et al., 2006; Patton et al., 2007). This test is highly accurate in detecting the multiple HIV-1 subtypes circulating in Africa (Stevens et al., 2008), is standardized and supported for use in Africa, and has been used by researchers and infant diagnosis pilot programs in several countries (Creek et al., 2007). However, Amplicor HIV-1 DNA PCR 1.5 uses primers for the relatively variable *gag* gene and was developed to amplify HIV-1 group M strains (Roche Diagnostics). So, it is likely that sensitivity problems arise with groups O, N and P. New DNA amplification assays that cover all HIV-1 genetic forms are needed

### 5. Impact of HIV-1 diversity in response to antiretroviral therapy

Differences in amino acid composition between HIV-1 clades can lead to differences in susceptibility to ARV drugs. This is best illustrated by HIV-1 group O and HIV-2 isolates that show high-level of innate resistance to NNRTIs and T20 (Descamps et al., 1997; Poveda et al., 2004; Smith et al., 2009). This innate resistance is due to resistance mutations that are present as natural polymorphisms. For instance, HIV-1 group O isolates naturally present a cysteine at RT position 181 (Y181C) which is considered a major drug resistance mutation (DRM) to NNRTIs; the secondary NNRTI DRM A98G is also a natural polymorphism in group O (Descamps et al., 1997; Poveda et al., 2004) (Table 3).

Susceptibility of non-B subtypes to ARV drugs has been less well studied than subtype B mainly because of the predominance of subtype B in developed countries where ARVs first became available, coupled with the availability of genotypic and phenotypic ARV drug resistance testing (Brenner, 2007). Some studies of sdNVP for prevention of MTCT have demonstrated a statistically significant disparity in the overall drug resistance among subtypes, with frequencies of 69-87%, 55.3-36%, 19-42%, and 21% resistance against NVP in women with subtypes C, D, A, and CRF02\_AG infections, respectively (Eshleman et al., 2005b; Flys et al., 2006; Johnson et al., 2005; Toni et al., 2005). There were no significant differences in the pre-NVP frequency of NVP resistance mutations or the pre-NVP levels of K103N-containing variants in women with subtypes A, C, and D that could explain the subtype-based differences in mutations after sdNVP exposure (Flys et al., 2006). However, there are other factors that may be associated with NVP resistance in women after the administration of sdNVP and which include: higher viral load and lower CD4+ T cell count prior to NVP exposure, increased pharmacokinetic exposure to NVP (e.g., longer half-life and decreased oral clearance of NVP), and the timing of sample collection (Eshleman et al., 2005b). Additional studies are needed that take in account all these factors to better understand the biological causes of these subtype differences in sdNVP resistance.

In the Pediatric European Network for Treatment of AIDS (PENTA) 5 trial, where 128 children were enrolled in a randomised trial to evaluate the antiviral effect of NRTI combinations (3TC+Abacavir, 3TC+ZDV, Abacavir+ZDV) and the tolerability of adding NFV, there was no significant difference according to HIV-1 subtype in the virologic response to treatment or in the frequency of development of resistance among children (Pillay et al., 2002). A French cohort study of 416 adult patients, 24% of whom carried non-B subtypes, showed that at 3, 6 and 12 months after initiation of ARV therapy (first line

regimens, subtype B: 65% PI-based regimens, 25% NNRTI-based regimens, 10% NRTI only; non-B subtype: 65% PI-based regimens, 30% NNRTI-based regimens, 5% NRTI only) HIV-1 subtype did not affect clinical progression, CD4 cell count, or viral load in response to treatment (Bocket et al., 2005). Frater *et al.* studied patients of African origin who were infected with a non-B subtype of HIV-1 and were living in London, and found no significant difference in the response to therapy (first line regimens, 50% PI-based regimens, 50% NNRTI-based regimens) among patients infected with subtypes A, C and D (Frater et al., 2001). Geretti and collaborators reported that patients infected with subtypes A, C, D and CRF02\_AG were as likely to achieve viral load suppression (NRTI backbone: AZT+3TC or TDF+FTC or TDF+3TC or 3TC+d4T or d4T+ddI or ABC+3TC; third drug: EFV or NVP or RTV boosted PI) as those infected with subtype B and showed comparable rates of CD4 cell count recovery (Geretti et al., 2009). Other studies have analyzed virologic and immunologic responses to antiretroviral therapy according to the HIV-1 subtype and also did not find any differences (Alexander et al., 2002; Atlas et al., 2005; Bannister et al., 2006; De Wit et al., 2004; Nicastrì et al., 2004). Thus, overall, it appears that HIV-1 subtypes do not have major differences in the response to ARV therapy. However, further studies should be designed, firstly to assess the efficacy of specific drug regimens in patients with non-B subtypes and secondly to evaluate the efficacy of these regimens in patients infected with particular non-B subtype species including the highly divergent H, J and K subtypes, complex CRFs and URFs which are common in African countries as well as in patients infected with group O, N and P viruses. These studies should be performed within a single country in order to control for the many variables that might influence response to therapy, namely, adherence, ethnicity, psychosocial support and drug regimens.

Polymorphisms	Prevalence in subtype B	Prevalence in non-B subtypes
A98S	5%	70% G and 98% O
K103R	2.7%	98% O
V179E	0.4%	98% O
V179I	3.2%	50% A
Y181C	0%	100% O

Adapted from (Wainberg and Brenner, 2010).

Table 3. Polymorphisms in the RT that may impact HIV-1 resistance to NNRTIs

## 6. Impact of HIV-1 diversity in drug resistance

In the absence of any drug exposure, RT and PR sequences from B and non-B subtypes are polymorphic in about 40% of the first 240 RT amino acids and 30% of the 99 PR amino acids (Bartolo et al., 2009b; Bartolo et al., 2009c; Kantor and Katzenstein, 2004). Polymorphisms in the RT of non-B subtype viruses normally do not occur in known sites of resistance to NRTIs (Kantor and Katzenstein, 2003); in contrast, the PR from drug naive patients may contain amino acid substitutions associated with secondary resistance to some PIs in subtype B (ex. K20R, M36I, H69KQ) (Table 4) (Grossman et al., 2001; Holguin et al., 2004). However, these genotypic changes by themselves do not consistently confer decreased susceptibility to PIs when viral strains are subject to phenotypic testing (Descamps et al., 2005; Grossman et al., 2004; Ly et al., 2005; Maljkovic et al., 2003; Nkengafac et al., 2007; Palma et al., 2007; Paraskevis et al., 2005; Roudinskii et al., 2004; Tee, Kamarulzaman, and Ng, 2006; Vazquez

de Parga et al., 2005; Wensing et al., 2005). Consistent with this, most observational studies performed *in vitro* and *in vivo* suggest that the currently available PR and RT inhibitors are as active against non-B subtype viruses as they are against subtype B viruses (Santos and Soares, 2010).

Different HIV genetic forms carry in their genomes genetic signatures and polymorphisms that could alter the structure of viral proteins which are targeted by drugs, thus impairing ARV drug binding and efficacy (Tables 3 and 4). A single nucleotide substitution from the wild-type codon found in subtype C can generate the mutation V106M, which is associated with NNRTIs resistance, while at least two substitutions are needed for the wild-type subtype B codon (Brenner et al., 2003; Loemba et al., 2002). This suggested that subtype C could have a lower genetic barrier to resistance to NNRTIs than subtype B, and that this V106M mutation could be more frequent in subtype C infected patients failing therapy, than in subtype B infected patients. Indeed, the clinical importance of the V106M mutation in non-B subtypes has been confirmed in several studies showing that V106M is more frequently seen in subtype C (and CRF01\_AE) after therapy with EFV or NVP (Deshpande et al., 2007; Hsu et al., 2005; Marconi et al., 2008; Rajesh et al., 2009). The G190A mutation was also relatively more frequent in subtype C Indian and Israeli patients failing NNRTI-based regimens than in subtype B (Deshpande et al., 2007; Grossman et al., 2004).

*In vitro*, the emergence of the K65R mutation after therapy with TDF is faster in subtype C (15 weeks after TDF) than in subtype B (34-74 weeks) (Brenner et al., 2006; Coutsinos et al., 2010; Coutsinos et al., 2009). In contrast, K65R may be less frequent in subtype A than in all other subtypes (Gupta et al., 2005). Several studies suggest that there is a higher risk of development of K65R in subtype C infected patients failing ddI and d4T-containing regimens (Brenner and Coutsinos, 2009; Deshpande et al., 2010; Doualla-Bell et al., 2006; Hosseinipour et al., 2009; Orrell et al., 2009). A study from Israel reported a high frequency of K65R in subtype C viruses from Ethiopian immigrants in ARV therapy (Turner et al., 2009). However, K65R did not appear to emerge frequently in subtype C patients who participated in large clinical trials in which they received either TDF or TDF/FTC as part of a triple therapy regimen (Miller et al., 2007). In Malawi, in patients with subtype C viruses, differences observed in the emergence of the K65R mutation were significantly related to treatment regimen and disease stage (Hosseinipour et al., 2009). In addition, development of K65R in subtype C and CRF01\_AE has been associated with the Y181C NVP mutation within the viral backbone (Brenner and Coutsinos, 2009; Zolfo et al., 2010 Set 22 [Epub ahead of print]). The presence of higher rates of the K65R mutation in subtype C in some studies (Doualla-Bell et al., 2006; Hosseinipour et al., 2009; Orrell et al., 2009) suggests that these viruses may have a particular predisposition toward acquiring this mutation. It has been proposed that a RNA template mechanism could explain the higher rates of K65R in subtype C viruses than in other subtypes. In this subtype, there is an intrinsic difficulty in synthesizing pol-A homopolymeric sequences that leads to template pausing at codon 65, facilitating the acquisition of K65R under selective drug pressure (Coutsinos et al., 2010; Coutsinos et al., 2009). The natural polymorphisms found in the RT of treatment-naive patients (10% in 726 patients) infected with HIV-1 non-B subtypes had no significant impact on susceptibility to ETR (Cotte et al., 2009; Derache et al., 2008; Maiga et al., 2010).

In PR, polymorphisms do not impair drug susceptibility but may affect the genetic pathway of resistance as soon as the virus generates a major resistant mutation (Martinez-Cajas et al., 2008). The rare minor V11I mutation, which is associated with DRV resistance, is a natural polymorphism in all CRF37\_cpx isolates and some subtype A isolates (Bartolo et al., 2009b; Bartolo et al., 2009c; de Meyer et al., 2008; Poveda et al., 2007; Powell et al., 2007a), suggesting that these viruses may have a lower genetic barrier to DRV resistance. The V82I natural polymorphism in subtype G led to the emergence of I82M/T/S with treatment failure to IDV (Camacho et al., 2005). A study suggested that polymorphisms at position 36 in PR may play important roles in determining the emergence of specific patterns of resistance mutations among viruses of different subtypes (Lisovsky et al., 2010). González *et al.* (Gonzalez et al., 2003) compared clinical isolates of C subtype with and without the I93L polymorphism, finding that hypersusceptibility to LPV in subtype C is strongly associated with the presence of that mutation.

Minor mutations	ARV	Prevalence in subtype B	Prevalence in non-B viruses
V11I	DRV	1%	100% CRF37_cpx and 4% in subtype A
I13V	TPV	13%	90%–98% in subtypes A, G and CRF02_AG, 4%–78% in other non-B subtypes
K20I	ATV	2%	93%–98% in subtypes G and CRF02_AG, 1%–3.5% in subtypes A, F and CRF01_AE
M36I	ATV, IDV, NFV and TPV	13%	81%–99% in several non-B subtypes
H69K	TPV	2%	96%–97% in subtypes A, C and G, CRF01_AE and CRF02_AG, 2% in subtype F
V82I	ATV	2%	87% in subtype G, 1%–6% in several non-B subtypes
I93L	ATV	33%	94% in subtype C, 5%–40% in several non-B subtypes

DRV, darunavir; TPV, tripranavir; ATV, atazanavir; IDV, indinavir; NFV, nelfinavir. Adapted from (Santos and Soares, 2010).

Table 4. Polymorphisms on the PR of HIV-1 non-B subtypes associated with resistance to PIs

The D30N mutation was not observed in CRF02\_AG and CRF02\_AE isolates from patients failing NFV therapy; rather, the N88S mutation emerged after NFV use in CRF01\_AE and after IDV use in subtype B (Ariyoshi et al., 2003; Chaix et al., 2005). The M89I/V mutations have been observed in C, F and G subtypes in PI experienced patients (NFV, APV, IDV, LPV, ATV) but not in other subtypes (Abecasis et al., 2005). The L90M mutation, that confers resistance to NFV and SQV, is rare in subtype F but common in subtype B in patients from Brazil (Calazans et al., 2005). D30N has a stronger negative impact in the replicative capacity

of C subtype than in B subtype (Gonzalez et al., 2004), which could explain the low frequency of this mutation observed in subtype C infected individuals failing NFV-containing regimens. A recent study in Portuguese patients, reported that mutation I54V/L was selected by NFV in subtype G isolates, a mutation not previously described for this drug in subtype B (Santos et al., 2009).

The frequency of polymorphisms in gp41 among different HIV-1 clades from T20 drug-naive patients is higher in non-B subtypes and recombinants than in subtype B viruses ( $P < 0.001$ ) especially at positions Q32L/T/N/K, R46K/Q, N43H, I37L, and V69L that are associated with resistance to T20 (Carmona et al., 2005). The N42S polymorphism, associated with increased susceptibility to T20, is detected more frequently in non-B subtypes than in B subtype (13% in B, 73% in A and 90% in G) (Carmona et al., 2005). A30V (in subtype G and CRF06\_cpx) and Q56K/R (in subtypes A and J, CRF04\_cpx, CRF09\_cpx, CRF11\_cpx, and CRF13\_cpx), Q56R and S138A in group O, and S138A in group N are natural polymorphisms associated with T20 resistance (Holguin, De Arellano, and Soriano, 2007).

Integrase inhibitor-associated mutations (primary and secondary) are normally absent from HIV-1 subtype B isolates from patients receiving ARV regimens without raltegravir (RAL) and from untreated patients (Ceccherini-Silberstein et al., 2010a; Ceccherini-Silberstein et al., 2010b). A study found integrase gene polymorphisms present in more than 10% of the 97 analyzed sequences (subtype B and non-B) from patients treated with RAL but these polymorphisms showed no impact on virological outcome either at week 24 or at week 48 (Charpentier et al., 2010). N155H, Q148H/R/K with G140S/A, and Y143R/C are the described mutational patterns that confer resistance to RAL, with or without secondary mutations (Garrido et al., 2010). A study on natural polymorphisms and mutations associated with resistance to RAL in drug-naive and ARV-treated patients (all RAL naive) found that CRF02\_AG and subtype C isolates could have a higher genetic barrier to the development of G140C or G140S compared to subtype B (Brenner et al., 2011). On group O viruses, natural presence of the E157Q mutation or E157E/Q mixture seems to confer resistance to RAL (Leoz et al., 2008).

These observations in non-B subtype viruses suggest that differences in drug resistance pathways between HIV-1 subtypes do exist. However, the accumulated evidence is insufficient to adequately assess the contribution of the innate genetic diversity of HIV-1 to resistance. Larger and more rigorous prospective studies in drug naive and treated patients are required to validate these hypotheses and it will be necessary to evaluate these mutations by the analysis of site-directed mutants in phenotypic resistance assays.

## **7. Impact of HIV-1 diversity in the performance of genotypic and phenotypic drug resistance assays**

Drug resistance testing is extremely important for the management of ART therapy failure in HIV patients (Grant and Zolopa, 2009; Shafer, 2002; Taylor, Jayasuriya, and Smit, 2009). Genotypic and phenotypic assays are both used to detect resistance to ARV drugs that could compromise response to treatment (Vandamme et al., 2011). All current clinically used genotypic assays involve sequencing the genes whose proteins are targeted by the different antiretroviral drugs [*pol* (RT, PR and IN) and *env*], to detect mutations that are known to

confer phenotypic drug resistance. There are two approved genotyping resistance assays commercially available, the ViroSeq HIV-1 genotyping system, version 2.0 (Eshleman et al., 2004) and the Trugene HIV-1 genotyping kit for drug resistance (Grant et al., 2003). Phenotypic assays measure the ability of an HIV-1 isolate to grow *in vitro* in the presence of an inhibitor, in comparison with a known susceptible strain.

The European HIV Drug Resistance Guidelines Panel recommends genotyping in most situations using updated and clinically evaluated interpretation systems (Vandamme et al., 2011). Genotypic assays are faster and cheaper than phenotypic assays (Vandamme et al., 2004). Nonetheless, the commercial genotypic tests are too expensive to be used in low-income countries. In-house methods for genotyping drug resistance mutations are recommended by WHO for surveillance of primary and secondary drug resistance (Bennett et al., 2008). The reported rate of success in amplification and sequencing with these methods in low-income countries ranges from 41 up to 100 % with non-B isolates (Bartolo et al., 2009b; Bartolo et al., 2009c; Bennett et al., 2008; Oliveira et al., 2011).

Several studies analyzed the performance of commercially available genotypic resistance assays and in-house methods in B and non-B strains (Aghokeng et al., 2011; Beddows et al., 2003; Fontaine et al., 2001; Jagodzinski et al., 2003; Maes et al., 2004). In commercial kits a greater degree of success was obtained when sequencing subtype B isolates compared to non-B isolates, and some studies report that alternative amplification/sequencing primers had to be used for some samples belonging to non-B subtypes. A Belgian study analyzed the performance of the ViroSeq HIV-1 Genotyping System in 383 samples comprising 12 different subtypes (Maes et al., 2004). Amplification failed in 8.4% of the samples and there was a lower performance in the amplification of non-B subtypes. The sequencing performance on the different subtypes showed a significant decrease of positive results for subtypes A, G and recombinant strains. As a result of sequencing problems, 18.5% of the samples had to be processed with in-house procedures. In Cameroon, where all groups of HIV-1 circulate, the sequencing efficiency of the ViroSeq assay was also evaluated (Aghokeng et al., 2011). The sequencing failures involved mainly the 5' end of the PR and the 3' end of the RT genes because of the high failure rate of primers A, D, F, and H. There was a high degree of polymorphism in non-B isolates in the areas for which these primers are designed. One study compared the two commercially available sequencing kits with a in-house genotyping system in HIV-1 samples from treated and untreated patients belonging to subtypes A through J (Fontaine et al., 2001). All the samples could be amplified and sequenced by the three systems; however, for all systems, alternative amplification/sequencing primers had to be used for some samples belonging to non-B subtypes.

Several studies have evaluated the use of DBS for HIV-1 genotypic resistance testing (reviewed in (Johannessen, 2010)). Nucleotide similarity between the two sample types ranged from 98.1 to 99.9%. Drug-resistant mutations found in plasma were detected in 82–100% of the corresponding DBS specimens. In all, these findings indicate that the performance of amplification and sequencing primers must be improved to allow good sequencing results and consequently fast and reliable resistance testing for all HIV-1 genetic forms. Validated in-house methods with primers designed on the basis of the local HIV genetic diversity are needed for low-resources settings.



Drug resistance interpretation algorithms are user friendly and helpful in the clinical setting to follow up HIV-infected patients. These algorithms have been developed to interpret complex patterns of resistance mutations in HIV-1 subtype B. The most frequently used clinically available systems are listed in Table 5. There are two types of systems, geno2pheno and *VirtualPhenotype* which try to predict viral phenotype under the assumption that phenotype predicts treatment response, whereas all other algorithms try primarily to predict treatment response based on information extracted from databases of genotypic and correlated phenotypic or treatment response data (Vandamme et al., 2011). Several studies have compared these algorithms in drug naive and treated patients infected with non-B subtypes to examine the influence of pre-existing polymorphisms on predictions of drug susceptibilities and the subsequent choice of therapy (Champenois et al., 2008; Depatureaux et al., 2011; Snoeck et al., 2006; Vergne et al., 2006a; Vergne et al., 2006b; Yebra et al., 2009). Most of these studies found some discordance between algorithms, which was related to the presence of naturally occurring polymorphisms in non-B subtypes (Champenois et al., 2008; Depatureaux et al., 2011; Snoeck et al., 2006; Vergne et al., 2006a; Vergne et al., 2006b; Yebra et al., 2009). A study showed that, according to available resistance algorithms, both B and non-B subtypes from drug naive patients were considered fully susceptible to PIs, except for TPV/RTV for which the ANRS algorithm scored non-B subtypes as naturally resistant (Champenois et al., 2008). The discordant results for TPV/RTV were due to differences in the mutations that are considered by the algorithms in the analysis. The ANRS algorithm takes in account TPV/RTV mutations that are considered natural polymorphisms in non-B subtypes (e.g. M36I, H69K and L89M). In another study, 68 drug naive and 9 highly ARV-experienced HIV-1 group O infected patients were analyzed (Depatureaux et al., 2011). Twelve minor resistance mutations, present in more than 75% of the PR sequences, led to the different algorithms giving discrepant results for NFV and SQV susceptibility.

A large study (5030 patients infected with different HIV-1 clades) found that the four algorithms analyzed agreed well on the level of resistance scored and that the discordances could be attributed to specific (subtype-dependent) combinations of mutations (Snoeck et al., 2006). In a comparison of five algorithms in HIV-1 sequences from drug naive patients, discordances were significantly higher in non-B vs. B variants for ddI, NVP, TPV, and fAPV, and were attributed to natural patterns of mutations in non-B subtypes (Yebra et al., 2009). Several other studies demonstrated that there was a lack of concordance between algorithms that predict treatment response based on phenotype and genotype (Holguin, Hertogs, and Soriano, 2003; Ross et al., 2005; Santos et al., 2009). These discrepancies indicate that the patterns of drug resistance mutations have not yet been completely clarified in non-B subtype variants. The use of certain algorithms could lead to an overestimation of the resistance in the analysis of specific non-B subtypes because of the lack of consensus in the resistance mutations considered although with increasing knowledge such discrepancies tend to diminish.

Tropism testing is recommended before the use of a CCR5 antagonist drug (Vandekerckhove et al., 2011). In general, the enhanced sensitivity Trofile (ESTA) assay (phenotypic assay) and V3 population genotyping are the recommended methods. A multicenter prospective study evaluated the performance of genotypic algorithms for prediction of HIV-1 coreceptor usage in comparison with a phenotypic assay for the determination of coreceptor usage (Recordon-Pinson et al., 2010). Researchers reported important differences between 13 algorithms in the sensitivity of detection of X4 isolates.

The most sensitive were PSSM and Geno2pheno, with sensitivities of about 60%; on the other hand the specificity was high for most algorithms. In other studies, higher sensitivities could be found for the same genotypic algorithms (Chueca et al., 2009; Raymond et al., 2008). Geno2pheno presented sensitivities of 88-93.7% and specificity of 87%, and PSSM with sensitivities of 77% and specificity of 94%. Overall, these studies validate genotypic algorithms for prediction of HIV-1 coreceptor use in antiretroviral-experienced patients infected with subtype B. Few studies have evaluated the performance of genotypic algorithms for prediction of HIV-1 coreceptor use in non-B subtype viruses. An initial report showed a poor performance of genotypic tools for non-B subtypes (A-J, CRF01\_AE, CRF02\_AG, CRF11, CRF12\_BF, CRF14\_BG, URFs, and U samples), where they particularly failed to detect X4 strains (Garrido et al., 2008). Other studies found that main genotypic algorithms perform well when applied to CRF02\_AG (Raymond et al., 2009) and subtype C viruses (Raymond et al., 2010). Additional studies are needed to evaluate the performance of these genotypic tools to predict coreceptor use in non-B subtypes.

System	Levels of resistance	Web Site
HIV DB Stanford	S, PL, LL, IR, HR	<a href="http://hivdb.stanford.edu/">http://hivdb.stanford.edu/</a>
REGA	S, I, R	<a href="http://www.kuleuven.ac.be/regacev/links/">http://www.kuleuven.ac.be/regacev/links/</a>
ANRS	S, I, R	<a href="http://www.hivfrenchresistance.org/index.html">http://www.hivfrenchresistance.org/index.html</a>
GenoSure	S, RP, R	<a href="http://www.monogramhiv.com">http://www.monogramhiv.com</a>
ResRis	S, I, R	<a href="http://www.retic-ris.net">http://www.retic-ris.net</a>
HIVGrade	S, I, LS, R	<a href="http://www.hiv-grade.de">http://www.hiv-grade.de</a>
AntiRetroScan	100/75/50/25/0#	<a href="http://www.hivarc.net/includeGenpub/AntiRetroScan.html">http://www.hivarc.net/includeGenpub/AntiRetroScan.html</a>
HIV-TRePS	Quantitative*	<a href="http://www.eurist.org">http://www.eurist.org</a>
EuResist Network	Quantitative*	<a href="http://www.eurist.org">http://www.eurist.org</a>
Geno2pheno	Quantitative, S, I, R	<a href="http://www.geno2pheno.org">http://www.geno2pheno.org</a>
Virco	Quantitative+	<a href="http://www.vircolab.com">http://www.vircolab.com</a>
ViroSeq	S, P, R	<a href="http://www.abbotmolecular.com">http://www.abbotmolecular.com</a>
TruGene	S, I, R	<a href="http://www.labnews.com">http://www.labnews.com</a>

S, susceptible; PL, possible low-level resistance; LL, low-level resistance; IR or I, intermediate resistance; HR, high level resistance; R, resistance; RP or P, resistance possible; LS, low susceptibility; #100/75/50/25/0 in %activity with drug-GSS weighting factor; \*probability for short-term response with specific drug combinations; +lower clinical cut-off at 20% of loss of response, upper to 80%. Adapted from (Vandamme et al., 2011).

Table 5. Drug resistance interpretation algorithms

## 8. References

Abecasis, A. B., Deforche, K., Snoeck, J., Bachelier, L. T., McKenna, P., Carvalho, A. P., Gomes, P., Camacho, R. J., and Vandamme, A. M. (2005). Protease mutation M89I/V is linked to therapy failure in patients infected with the HIV-1 non-B subtypes C, F or G. *AIDS* 19(16), 1799-806.

- Abecasis, A. B., Martins, A., Costa, I., Carvalho, A. P., Diogo, I., Gomes, P., and Camacho, R. J. (2011). Molecular epidemiological analysis of paired pol/env sequences from Portuguese HIV type 1 patients. *AIDS Res Hum Retroviruses* 27(7), 803-5.
- Adojaan, M., Kivisild, T., Mannik, A., Krispin, T., Ustina, V., Zilmer, K., Liebert, E., Jaroslavtsev, N., Priimagi, L., Tefanova, V., Schmidt, J., Krohn, K., VILLEMS, R., Salminen, M., and Ustav, M. (2005). Predominance of a rare type of HIV-1 in Estonia. *J Acquir Immune Defic Syndr* 39(5), 598-605.
- Aghokeng, A. F., Mpoudi-Ngole, E., Chia, J. E., Edoul, E. M., Delaporte, E., and Peeters, M. (2011). High failure rate of the ViroSeq HIV-1 genotyping system for drug resistance testing in Cameroon, a country with broad HIV-1 genetic diversity. *J Clin Microbiol* 49(4), 1635-41.
- Aghokeng, A. F., Mpoudi-Ngole, E., Dimodi, H., Atem-Tambe, A., Tongo, M., Butel, C., Delaporte, E., and Peeters, M. (2009). Inaccurate diagnosis of HIV-1 group M and O is a key challenge for ongoing universal access to antiretroviral treatment and HIV prevention in Cameroon. *PLoS One* 4(11), e7702.
- Ahmad, N. (2005). The vertical transmission of human immunodeficiency virus type 1: molecular and biological properties of the virus. *Crit Rev Clin Lab Sci* 42(1), 1-34.
- AIDSInfo (May 24, 2010). Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. <http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf>AIDSinfo.
- Akouamba, B. S., Viel, J., Charest, H., Merindol, N., Samson, J., Lapointe, N., Brenner, B. G., Lalonde, R., Harrigan, P. R., Boucher, M., and Soudeyins, H. (2005). HIV-1 genetic diversity in antenatal cohort, Canada. *Emerg Infect Dis* 11(8), 1230-4.
- Alaeus, A., Lidman, K., Bjorkman, A., Giesecke, J., and Albert, J. (1999). Similar rate of disease progression among individuals infected with HIV-1 genetic subtypes A-D. *AIDS* 13(8), 901-7.
- Alexander, C. S., Montessori, V., Wynhoven, B., Dong, W., Chan, K., O'Shaughnessy, M. V., Mo, T., Piaseczny, M., Montaner, J. S., and Harrigan, P. R. (2002). Prevalence and response to antiretroviral therapy of non-B subtypes of HIV in antiretroviral-naive individuals in British Columbia. *Antivir Ther* 7(1), 31-5.
- Amornkul, P. N., Tansuphasawadikul, S., Limpakarnjanarat, K., Likanonsakul, S., Young, N., Eampokalap, B., Kaewkungwal, J., Naiwatanakul, T., Von Bargen, J., Hu, D. J., and Mastro, T. D. (1999). Clinical disease associated with HIV-1 subtype B' and E infection among 2104 patients in Thailand. *AIDS* 13(14), 1963-9.
- Andreotti, M., Pirillo, M., Guidotti, G., Ceffa, S., Paturzo, G., Germano, P., Luhanga, R., Chimwaza, D., Mancini, M. G., Marazzi, M. C., Vella, S., Palombi, L., and Giuliano, M. (2010). Correlation between HIV-1 viral load quantification in plasma, dried blood spots, and dried plasma spots using the Roche COBAS Taqman assay. *J Clin Virol* 47(1), 4-7.
- Annaz, H., Recordon-Pinson, P., Baba, N., Sedrati, O., Mrani, S., and Fleury, H. (2011). Presence of Drug Resistance Mutations Among Drug-Naive Patients in Morocco. *AIDS Res Hum Retroviruses*.27 (8): 917-920.
- Apetrei, C., Loussert-Ajaka, I., Descamps, D., Damond, F., Saragosti, S., Brun-Vezinet, F., and Simon, F. (1996). Lack of screening test sensitivity during HIV-1 non-subtype B seroconversions. *AIDS* 10(14), F57-60.

- Ariyoshi, K., Matsuda, M., Miura, H., Tateishi, S., Yamada, K., and Sugiura, W. (2003). Patterns of point mutations associated with antiretroviral drug treatment failure in CRF01\_AE (subtype E) infection differ from subtype B infection. *J Acquir Immune Defic Syndr* 33(3), 336-42.
- Atlas, A., Granath, F., Lindstrom, A., Lidman, K., Lindback, S., and Alaeus, A. (2005). Impact of HIV type 1 genetic subtype on the outcome of antiretroviral therapy. *AIDS Res Hum Retroviruses* 21(3), 221-7.
- Attia, S., Egger, M., Muller, M., Zwahlen, M., and Low, N. (2009). Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS* 23(11), 1397-404.
- Avila, M. M., Pando, M. A., Carrion, G., Peralta, L. M., Salomon, H., Carrillo, M. G., Sanchez, J., Maulen, S., Hierholzer, J., Marinello, M., Negrete, M., Russell, K. L., and Carr, J. K. (2002). Two HIV-1 epidemics in Argentina: different genetic subtypes associated with different risk groups. *J Acquir Immune Defic Syndr* 29(4), 422-6.
- Bannister, W. P., Ruiz, L., Loveday, C., Vella, S., Zilmer, K., Kjaer, J., Knysz, B., Phillips, A. N., and Mocroft, A. (2006). HIV-1 subtypes and response to combination antiretroviral therapy in Europe. *Antivir Ther* 11(6), 707-15.
- Bártolo, I., Abecasis, A. B., Borrego, P., Barroso, H., McCutchan, F., Gomes, P., Camacho, R., and Taveira, N. (2011). Origin and Epidemiological History of HIV-1 CRF14\_BG. *PLoS ONE*, Accepted
- Bartolo, I., Camacho, R., Barroso, H., Bezerra, V., and Taveira, N. (2009a). Rapid clinical progression to AIDS and death in a persistently seronegative HIV-1 infected heterosexual young man. *AIDS* 23(17), 2359-62.
- Bartolo, I., Casanovas, J., Bastos, R., Rocha, C., Abecasis, A. B., Folgosa, E., Mondlane, J., Manuel, R., and Taveira, N. (2009b). HIV-1 genetic diversity and transmitted drug resistance in health care settings in Maputo, Mozambique. *J Acquir Immune Defic Syndr* 51(3), 323-31.
- Bartolo, I., Epalanga, M., Bartolomeu, J., Fonseca, M., Mendes, A., Gama, A., and Taveira, N. (2005). High genetic diversity of human immunodeficiency virus type 1 in Angola. *AIDS Res Hum Retroviruses* 21(4), 306-10.
- Bartolo, I., Rocha, C., Bartolomeu, J., Gama, A., Fonseca, M., Mendes, A., Cristina, F., Thamm, S., Epalanga, M., Silva, P. C., and Taveira, N. (2009c). Antiretroviral drug resistance surveillance among treatment-naive human immunodeficiency virus type 1-infected individuals in Angola: evidence for low level of transmitted drug resistance. *Antimicrob Agents Chemother* 53(7), 3156-8.
- Bartolo, I., Rocha, C., Bartolomeu, J., Gama, A., Marcelino, R., Fonseca, M., Mendes, A., Epalanga, M., Silva, P. C., and Taveira, N. (2009d). Highly divergent subtypes and new recombinant forms prevail in the HIV/AIDS epidemic in Angola: New insights into the origins of the AIDS pandemic. *Infect Genet Evol* 9, 672-682. .
- Beddows, S., Galpin, S., Kazmi, S. H., Ashraf, A., Johargy, A., Frater, A. J., White, N., Braganza, R., Clarke, J., McClure, M., and Weber, J. N. (2003). Performance of two commercially available sequence-based HIV-1 genotyping systems for the detection of drug resistance against HIV type 1 group M subtypes. *J Med Virol* 70(3), 337-42.
- Beelaert, G., and Fransen, K. (2010). Evaluation of a rapid and simple fourth-generation HIV screening assay for qualitative detection of HIV p24 antigen and/or antibodies to HIV-1 and HIV-2. *J Virol Methods* 168(1-2), 218-22.

- Bennett, D. E., Myatt, M., Bertagnolio, S., Sutherland, D., and Gilks, C. F. (2008). Recommendations for surveillance of transmitted HIV drug resistance in countries scaling up antiretroviral treatment. *Antivir Ther* 13 Suppl 2, 25-36.
- Beyrer, C., Patel, Z., Stachowiak, J. A., Tishkova, F. K., Stibich, M. A., Eyzaguirre, L. M., Carr, J. K., Mogilnii, V., Peryshkina, A., Latypov, A., and Strathdee, S. A. (2009). Characterization of the emerging HIV type 1 and HCV epidemics among injecting drug users in Dushanbe, Tajikistan. *AIDS Res Hum Retroviruses* 25(9), 853-60.
- (2009). Assays to Estimate HIV Incidence and Detect Acute HIV Infection. Bill & Melinda Gates Foundation.
- Bobkov, A., Cheingsong-Popov, R., Selimova, L., Ladnaya, N., Kazennova, E., Kravchenko, A., Fedotov, E., Saukhat, S., Zverev, S., Pokrovsky, V., and Weber, J. (1997). An HIV type 1 epidemic among injecting drug users in the former Soviet Union caused by a homogeneous subtype A strain. *AIDS Res Hum Retroviruses* 13(14), 1195-201.
- Bobkov, A. F., Kazennova, E. V., Sukhanova, A. L., Bobkova, M. R., Pokrovsky, V. V., Zeman, V. V., Kovtunencko, N. G., and Erasiloova, I. B. (2004). An HIV type 1 subtype A outbreak among injecting drug users in Kazakhstan. *AIDS Res Hum Retroviruses* 20(10), 1134-6.
- Bocket, L., Cheret, A., Deuffic-Burban, S., Choisy, P., Gerard, Y., de la Tribonniere, X., Viget, N., Ajana, F., Goffard, A., Barin, F., Mouton, Y., and Yazdanpanah, Y. (2005). Impact of human immunodeficiency virus type 1 subtype on first-line antiretroviral therapy effectiveness. *Antivir Ther* 10(2), 247-54.
- Bogh, M., Machuca, R., Gerstoft, J., Pedersen, C., Obel, N., Kvinesdal, B., Nielsen, H., and Nielsen, C. (2001). Subtype-specific problems with qualitative Amplicor HIV-1 DNA PCR test. *J Clin Virol* 20(3), 149-53.
- Bourlet, T., Signori-Schmuck, A., Roche, L., Icard, V., Saoudin, H., Trabaud, M. A., Tardy, J. C., Morand, P., Pozzetto, B., Ecochard, R., and Andre, P. (2011). HIV-1 load comparison using four commercial real-time assays. *J Clin Microbiol* 49(1), 292-7.
- Brennan, C. A., Bodelle, P., Coffey, R., Devare, S. G., Golden, A., Hackett, J., Jr., Harris, B., Holzmayr, V., Luk, K. C., Schochetman, G., Swanson, P., Yamaguchi, J., Vallari, A., Ndembi, N., Ngansop, C., Makamche, F., Mbanya, D., Gurtler, L. G., Zekeng, L., and Kaptue, L. (2008). The prevalence of diverse HIV-1 strains was stable in Cameroonian blood donors from 1996 to 2004. *J Acquir Immune Defic Syndr* 49(4), 432-9.
- Brennan, C. A., Bodelle, P., Coffey, R., Harris, B., Holzmayr, V., Luk, K. C., Swanson, P., Yamaguchi, J., Vallari, A., Devare, S. G., Schochetman, G., and Hackett, J., Jr. (2006). HIV global surveillance: foundation for retroviral discovery and assay development. *J Med Virol* 78 Suppl 1, S24-9.
- Brennan, C. A., Yamaguchi, J., Devare, S. G., Foster, G. A., and Stramer, S. L. (2010). Expanded evaluation of blood donors in the United States for human immunodeficiency virus type 1 non-B subtypes and antiretroviral drug-resistant strains: 2005 through 2007. *Transfusion* 50(12), 2707-12.
- Brenner, B., Oliveira, M., Doualla-Bell, F., Moisi, D., Ntemgwa, M., Frankel, F., Essex, M., and Wainberg, M. (2006). HIV-1 subtype C viruses rapidly develop K65R resistance to tenofovir in cell culture. *AIDS* 20(9), F9-13.
- Brenner, B., Turner, D., Oliveira, M., Moisi, D., Detorio, M., Carobene, M., Marlink, R. G., Schapiro, J., Roger, M., and Wainberg, M. A. (2003). A V106M mutation in HIV-1 clade C viruses exposed to efavirenz confers cross-resistance to non-nucleoside reverse transcriptase inhibitors. *AIDS* 17(1), F1-5.

- Brenner, B. G. (2007). Resistance and viral subtypes: how important are the differences and why do they occur? *Curr Opin HIV AIDS* 2(2), 94-102.
- Brenner, B. G., and Coutsinos, D. (2009). The K65R mutation in HIV-1 reverse transcriptase: genetic barriers, resistance profile and clinical implications. *HIV Ther* 3(6), 583-594.
- Brenner, B. G., Lowe, M., Moisi, D., Hardy, I., Gagnon, S., Charest, H., Baril, J. G., Wainberg, M. A., and Roger, M. (2011). Subtype diversity associated with the development of HIV-1 resistance to integrase inhibitors. *J Med Virol* 83(5), 751-9.
- Buonaguro, L., Tornesello, M. L., and Buonaguro, F. M. (2007). Human immunodeficiency virus type 1 subtype distribution in the worldwide epidemic: pathogenetic and therapeutic implications. *J Virol* 81, 10209-10219.
- Calazans, A., Brindeiro, R., Brindeiro, P., Verli, H., Arruda, M. B., Gonzalez, L. M., Guimaraes, J. A., Diaz, R. S., Antunes, O. A., and Tanuri, A. (2005). Low accumulation of L90M in protease from subtype F HIV-1 with resistance to protease inhibitors is caused by the L89M polymorphism. *J Infect Dis* 191(11), 1961-70.
- Camacho, R., Godinho, A., Gomes, P., Abecasis, A., Vandamme, A.-M., Palma, C., Carvalho, A., Cabanas, J., and Gonçalves, J. (2005). Different substitutions under drug pressure at protease codon 82 in HIV-1 subtype G compared to subtype B infected individuals including a novel I82M resistance mutation. *Antivir Ther.* 10, Suppl 1.
- Carmona, R., Perez-Alvarez, L., Munoz, M., Casado, G., Delgado, E., Sierra, M., Thomson, M., Vega, Y., Vazquez de Parga, E., Contreras, G., Medrano, L., and Najera, R. (2005). Natural resistance-associated mutations to Enfuvirtide (T20) and polymorphisms in the gp41 region of different HIV-1 genetic forms from T20 naive patients. *J Clin Virol* 32(3), 248-53.
- Carr, J. K., Osinusi, A., Flynn, C. P., Gilliam, B. L., Maheshwari, V., and Zhao, R. Y. (2010a). Two independent epidemics of HIV in Maryland. *J Acquir Immune Defic Syndr* 54(3), 297-303.
- Carr, J. K., Wolfe, N. D., Torimiro, J. N., Tamoufe, U., Mpoudi-Ngole, E., Eyzaguirre, L., Birx, D. L., McCutchan, F. E., and Burke, D. S. (2010b). HIV-1 recombinants with multiple parental strains in low-prevalence, remote regions of Cameroon: evolutionary relics? *Retrovirology* 7, 39.
- Casper, C., Naver, L., Clevestig, P., Belfrage, E., Leitner, T., Albert, J., Lindgren, S., Ottenblad, C., Bohlin, A. B., Fenyo, E. M., and Ehrnst, A. (2002). Coreceptor change appears after immune deficiency is established in children infected with different HIV-1 subtypes. *AIDS Res Hum Retroviruses* 18(5), 343-52.
- Castro, E., Khonkarly, M., Ciuffreda, D., Burgisser, P., Cavassini, M., Yerly, S., Pantaleo, G., and Bart, P. A. (2010). HIV-1 drug resistance transmission networks in southwest Switzerland. *AIDS Res Hum Retroviruses* 26(11), 1233-8.
- Ceccherini-Silberstein, F., Malet, I., Fabeni, L., Dimonte, S., Svicher, V., D'Arrigo, R., Artese, A., Costa, G., Bono, S., Alcaro, S., Monforte, A., Katlama, C., Calvez, V., Antinori, A., Marcelin, A. G., and Perno, C. F. (2010a). Specific HIV-1 integrase polymorphisms change their prevalence in untreated versus antiretroviral-treated HIV-1-infected patients, all naive to integrase inhibitors. *J Antimicrob Chemother* 65(11), 2305-18.
- Ceccherini-Silberstein, F., Van Baelen, K., Armenia, D., Trignetti, M., Rondelez, E., Fabeni, L., Scopelliti, F., Pollicita, M., Van Wesenbeeck, L., Van Eygen, V., Dori, L., Sarmati, L., Aquaro, S., Palamara, G., Andreoni, M., Stuyver, L. J., and Perno, C. F. (2010b). Secondary integrase resistance mutations found in HIV-1 minority quasispecies in

- integrase therapy-naive patients have little or no effect on susceptibility to integrase inhibitors. *Antimicrob Agents Chemother* 54(9), 3938-48.
- Chaillet, P., Tayler-Smith, K., Zachariah, R., Duclos, N., Moctar, D., Beelaert, G., and Fransen, K. (2010). Evaluation of four rapid tests for diagnosis and differentiation of HIV-1 and HIV-2 infections in Guinea-Conakry, West Africa. *Trans R Soc Trop Med Hyg* 104(9), 571-6.
- Chaix, M. L., Rouet, F., Kouakoussui, K. A., Laguide, R., Fassinou, P., Montcho, C., Blanche, S., Rouzioux, C., and Msellati, P. (2005). Genotypic human immunodeficiency virus type 1 drug resistance in highly active antiretroviral therapy-treated children in Abidjan, Cote d'Ivoire. *Pediatr Infect Dis J* 24(12), 1072-6.
- Champenois, K., Bocket, L., Deuffic-Burban, S., Cotte, L., Andre, P., Choisy, P., and Yazdanpanah, Y. (2008). Expected response to protease inhibitors of HIV-1 non-B subtype viruses according to resistance algorithms. *AIDS* 22(9), 1087-9.
- Charpentier, C., Roquebert, B., Colin, C., Taburet, A. M., Fagard, C., Katlama, C., Molina, J. M., Jacomet, C., Brun-Vezinet, F., Chene, G., Yazdanpanah, Y., and Descamps, D. (2010). Resistance analyses in highly experienced patients failing raltegravir, etravirine and darunavir/ritonavir regimen. *AIDS* 24(17), 2651-6.
- Chen, J. H., Wong, K. H., Chen, Z., Chan, K., Lam, H. Y., To, S. W., Cheng, V. C., Yuen, K. Y., and Yam, W. C. (2010). Increased genetic diversity of HIV-1 circulating in Hong Kong. *PLoS One* 5(8), e12198.
- Christopherson, C., Sninsky, J., and Kwok, S. (1997). The effects of internal primer-template mismatches on RT-PCR: HIV-1 model studies. *Nucleic Acids Res* 25(3), 654-8.
- Chueca, N., Garrido, C., Alvarez, M., Poveda, E., de Dios Luna, J., Zahonero, N., Hernandez-Quero, J., Soriano, V., Maroto, C., de Mendoza, C., and Garcia, F. (2009). Improvement in the determination of HIV-1 tropism using the V3 gene sequence and a combination of bioinformatic tools. *J Med Virol* 81(5), 763-7.
- Church, D., Gregson, D., Lloyd, T., Klein, M., Beckthold, B., Laupland, K., and Gill, J. (2011). HIV-1 Viral Load Multi-Assay Comparison of the RealTime HIV-1, COBAS TaqMan 48 v 1.0, Easy Q v1.2 and Versant v3.0 assays in a Cohort of Canadian Patients with Diverse HIV Subtype Infections. *J Clin Microbiol* 49(1), 118-124.
- Cilliers, T., Nhlapo, J., Coetzer, M., Orlovic, D., Ketas, T., Olson, W. C., Moore, J. P., Trkola, A., and Morris, L. (2003). The CCR5 and CXCR4 coreceptors are both used by human immunodeficiency virus type 1 primary isolates from subtype C. *J Virol* 77(7), 4449-56.
- Collins, M. L., Irvine, B., Tyner, D., Fine, E., Zayati, C., Chang, C., Horn, T., Ahle, D., Detmer, J., Shen, L. P., Kolberg, J., Bushnell, S., Urdea, M. S., and Ho, D. D. (1997). A branched DNA signal amplification assay for quantification of nucleic acid targets below 100 molecules/ml. *Nucleic Acids Res* 25(15), 2979-84.
- Conroy, S. A., Laeyendecker, O., Redd, A. D., Collinson-Streng, A., Kong, X., Makumbi, F., Lutalo, T., Sewankambo, N., Kiwanuka, N., Gray, R. H., Wawer, M. J., Serwadda, D., and Quinn, T. C. (2010). Changes in the distribution of HIV type 1 subtypes D and A in Rakai District, Uganda between 1994 and 2002. *AIDS Res Hum Retroviruses* 26(10), 1087-91.
- Cornelissen, M., van Den Burg, R., Zorgdrager, F., and Goudsmit, J. (2000). Spread of distinct human immunodeficiency virus type 1 AG recombinant lineages in Africa. *J Gen Virol* 81(Pt 2), 515-23.

- Cotte, L., Trabaud, M. A., Tardy, J. C., Brochier, C., Gilibert, R. P., Mialhes, P., Trepo, C., and Andre, P. (2009). Prediction of the virological response to etravirine in clinical practice: Comparison of three genotype algorithms. *J Med Virol* 81(4), 672-7.
- Coutsinos, D., Invernizzi, C. F., Xu, H., Brenner, B. G., and Wainberg, M. A. (2010). Factors affecting template usage in the development of K65R resistance in subtype C variants of HIV type-1. *Antivir Chem Chemother* 20(3), 117-31.
- Coutsinos, D., Invernizzi, C. F., Xu, H., Moisi, D., Oliveira, M., Brenner, B. G., and Wainberg, M. A. (2009). Template usage is responsible for the preferential acquisition of the K65R reverse transcriptase mutation in subtype C variants of human immunodeficiency virus type 1. *J Virol* 83(4), 2029-33.
- Creek, T. L., Sherman, G. G., Nkengasong, J., Lu, L., Finkbeiner, T., Fowler, M. G., Rivadeneira, E., and Shaffer, N. (2007). Infant human immunodeficiency virus diagnosis in resource-limited settings: issues, technologies, and country experiences. *Am J Obstet Gynecol* 197(3 Suppl), S64-71.
- De Mendoza, C., Garrido, C., Poveda, E., Corral, A., Zahonero, N., Trevino, A., Anta, L., and Soriano, V. (2009). Changes in drug resistance patterns following the introduction of HIV type 1 non-B subtypes in Spain. *AIDS Res Hum Retroviruses* 25(10), 967-72.
- de Mendoza, C., Koppelman, M., Montes, B., Ferre, V., Soriano, V., Cuypers, H., Segondy, M., and Oosterlaken, T. (2005). Multicenter evaluation of the NucliSens EasyQ HIV-1 v1.1 assay for the quantitative detection of HIV-1 RNA in plasma. *J Virol Methods* 127(1), 54-9.
- de Meyer, S., Vangeneugden, T., van Baelen, B., de Paepe, E., van Marck, H., Picchio, G., Lefebvre, E., and de Bethune, M. P. (2008). Resistance profile of darunavir: combined 24-week results from the POWER trials. *AIDS Res Hum Retroviruses* 24(3), 379-88.
- De Wit, S., Boulme, R., Poll, B., Schmit, J. C., and Clumeck, N. (2004). Viral load and CD4 cell response to protease inhibitor-containing regimens in subtype B versus non-B treatment-naive HIV-1 patients. *AIDS* 18(17), 2330-1.
- Depatureaux, A., Charpentier, C., Leoz, M., Unal, G., Damond, F., Kfutwah, A., Vessiere, A., Simon, F., and Plantier, J. C. (2011). Impact of HIV-1 Group O Genetic Diversity on Genotypic Resistance Interpretation by Algorithms Designed for HIV-1 Group M. *J Acquir Immune Defic Syndr* 56(2), 139-145.
- Derache, A., Maiga, A. I., Traore, O., Akonde, A., Cisse, M., Jarrousse, B., Koita, V., Diarra, B., Carcelain, G., Barin, F., Pizzocolo, C., Pizarro, L., Katlama, C., Calvez, V., and Marcelin, A. G. (2008). Evolution of genetic diversity and drug resistance mutations in HIV-1 among untreated patients from Mali between 2005 and 2006. *J Antimicrob Chemother* 62(3), 456-63.
- Descamps, D., Chaix, M. L., Andre, P., Brodard, V., Cottalorda, J., Deveau, C., Harzic, M., Ingrand, D., Izopet, J., Kohli, E., Masquelier, B., Mouajjah, S., Palmer, P., Pellegrin, I., Plantier, J. C., Poggi, C., Rogez, S., Ruffault, A., Schneider, V., Signori-Schmuck, A., Tamalet, C., Wirden, M., Rouzioux, C., Brun-Vezinet, F., Meyer, L., and Costagliola, D. (2005). French national sentinel survey of antiretroviral drug resistance in patients with HIV-1 primary infection and in antiretroviral-naive chronically infected patients in 2001-2002. *J Acquir Immune Defic Syndr* 38(5), 545-52.
- Descamps, D., Collin, G., Letourneur, F., Apetrei, C., Damond, F., Loussert-Ajaka, I., Simon, F., Saragosti, S., and Brun-Vezinet, F. (1997). Susceptibility of human immunodeficiency virus type 1 group O isolates to antiretroviral agents: in vitro phenotypic and genotypic analyses. *J Virol* 71(11), 8893-8.



- Deshpande, A., Jauvin, V., Magnin, N., Pinson, P., Faure, M., Masquelier, B., Aurillac-Lavignolle, V., and Fleury, H. J. (2007). Resistance mutations in subtype C HIV type 1 isolates from Indian patients of Mumbai receiving NRTIs plus NNRTIs and experiencing a treatment failure: resistance to AR. *AIDS Res Hum Retroviruses* 23(2), 335-40.
- Deshpande, A., Jeannot, A. C., Schrive, M. H., Wittkop, L., Pinson, P., and Fleury, H. J. (2010). Analysis of RT sequences of subtype C HIV-type 1 isolates from Indian patients at failure of a first-line treatment according to clinical and/or immunological WHO guidelines. *AIDS Res Hum Retroviruses* 26(3), 343-50.
- Dickover, R., Garratty, E., Yusim, K., Miller, C., Korber, B., and Bryson, Y. (2006). Role of maternal autologous neutralizing antibody in selective perinatal transmission of human immunodeficiency virus type 1 escape variants. *J Virol* 80(13), 6525-33.
- Dickover, R. E., Garratty, E. M., Plaeger, S., and Bryson, Y. J. (2001). Perinatal transmission of major, minor, and multiple maternal human immunodeficiency virus type 1 variants in utero and intrapartum. *J Virol* 75(5), 2194-203.
- Djoko, C. F., Rimoin, A. W., Vidal, N., Tamoufe, U., Wolfe, N. D., Butel, C., Lebreton, M., Tshala, F. M., Kayembe, P. K., Muyembe, J. J., Edidi-Basepeo, S., Pike, B. L., Fair, J. N., Mbacham, W. F., Saylor, K. E., Mpoudi-Ngole, E., Delaporte, E., Grillo, M., and Peeters, M. (2011). High HIV Type 1 Group M pol Diversity and Low Rate of Antiretroviral Resistance Mutations Among the 13 Uniformed Services in Kinshasa, DRC. *AIDS Res Hum Retroviruses* 27 (3): 323-329.
- Doualla-Bell, F., Avalos, A., Brenner, B., Gaolathe, T., Mine, M., Gaseitsiwe, S., Oliveira, M., Moisi, D., Ndwapi, N., Moffat, H., Essex, M., and Wainberg, M. A. (2006). High prevalence of the K65R mutation in human immunodeficiency virus type 1 subtype C isolates from infected patients in Botswana treated with didanosine-based regimens. *Antimicrob Agents Chemother* 50(12), 4182-5.
- Dumans, A. T., Soares, M. A., Machado, E. S., Hue, S., Brindeiro, R. M., Pillay, D., and Tanuri, A. (2004). Synonymous genetic polymorphisms within Brazilian human immunodeficiency virus Type 1 subtypes may influence mutational routes to drug resistance. *J Infect Dis* 189(7), 1232-8.
- Dyer, J. R., Pilcher, C. D., Shepard, R., Schock, J., Eron, J. J., and Fiscus, S. A. (1999). Comparison of NucliSens and Roche Monitor assays for quantitation of levels of human immunodeficiency virus type 1 RNA in plasma. *J Clin Microbiol* 37(2), 447-9.
- Easterbrook, P. J., Smith, M., Mullen, J., O'Shea, S., Chrystie, I., de Ruiter, A., Tatt, I. D., Geretti, A. M., and Zuckerman, M. (2010). Impact of HIV-1 viral subtype on disease progression and response to antiretroviral therapy. *J Int AIDS Soc* 13, 4.
- Eberle, J., LouSSERT-Ajaka, I., Brust, S., Zekeng, L., Hauser, P. H., Kaptue, L., Knapp, S., Damond, F., Saragosti, S., Simon, F., and Gurtler, L. G. (1997). Diversity of the immunodominant epitope of gp41 of HIV-1 subtype O and its validity for antibody detection. *J Virol Methods* 67(1), 85-91.
- Eshleman, S. H., Church, J. D., Chen, S., Guay, L. A., Mwatha, A., Fiscus, S. A., Mmiro, F., Musoke, P., Kumwenda, N., Jackson, J. B., Taha, T. E., and Hoover, D. R. (2006). Comparison of HIV-1 mother-to-child transmission after single-dose nevirapine prophylaxis among African women with subtypes A, C, and D. *J Acquir Immune Defic Syndr* 42(4), 518-21.
- Eshleman, S. H., Guay, L. A., Mwatha, A., Brown, E., Musoke, P., Mmiro, F., and Jackson, J. B. (2005a). Comparison of mother-to-child transmission rates in Ugandan women

- with subtype A versus D HIV-1 who received single-dose nevirapine prophylaxis: HIV Network For Prevention Trials 012. *J Acquir Immune Defic Syndr* 39(5), 593-7.
- Eshleman, S. H., Hackett, J., Jr., Swanson, P., Cunningham, S. P., Drews, B., Brennan, C., Devare, S. G., Zekeng, L., Kaptue, L., and Marlowe, N. (2004). Performance of the Celera Diagnostics ViroSeq HIV-1 Genotyping System for sequence-based analysis of diverse human immunodeficiency virus type 1 strains. *J Clin Microbiol* 42(6), 2711-7.
- Eshleman, S. H., Hoover, D. R., Chen, S., Hudelson, S. E., Guay, L. A., Mwatha, A., Fiscus, S. A., Mmiro, F., Musoke, P., Jackson, J. B., Kumwenda, N., and Taha, T. (2005b). Nevirapine (NVP) resistance in women with HIV-1 subtype C, compared with subtypes A and D, after the administration of single-dose NVP. *J Infect Dis* 192(1), 30-6.
- Esteves, A., Parreira, R., Piedade, J., Venenno, T., Franco, M., Germano de Sousa, J., Patricio, L., Brum, P., Costa, A., and Canas-Ferreira, W. F. (2003). Spreading of HIV-1 subtype G and envB/gagG recombinant strains among injecting drug users in Lisbon, Portugal. *AIDS Res Hum Retroviruses* 19(6), 511-7.
- Esteves, A., Parreira, R., Venenno, T., Franco, M., Piedade, J., Germano De Sousa, J., and Canas-Ferreira, W. F. (2002). Molecular epidemiology of HIV type 1 infection in Portugal: high prevalence of non-B subtypes. *AIDS Res Hum Retroviruses* 18(5), 313-25.
- European AIDS Clinical Society (2009). Guidelines for the clinical management and treatment of HIV-infected adults in Europe. European AIDS Clinical Society.
- Eyzaguirre, L. M., Erasilova, I. B., Nadai, Y., Saad, M. D., Kovtunencko, N. G., Gomatos, P. J., Zeman, V. V., Botros, B. A., Sanchez, J. L., Birx, D. L., Earhart, K. C., and Carr, J. K. (2007). Genetic characterization of HIV-1 strains circulating in Kazakhstan. *J Acquir Immune Defic Syndr* 46(1), 19-23.
- Fernandez-Garcia, A., Cuevas, M. T., Vinogradova, A., Rakhmanova, A., Perez-Alvarez, L., de Castro, R. O., Osmanov, S., and Thomson, M. M. (2009). Near full-length genome characterization of a newly identified HIV type 1 subtype F variant circulating in St. Petersburg, Russia. *AIDS Res Hum Retroviruses* 25(11), 1187-91.
- Ferreira Junior, O. C., Ferreira, C., Riedel, M., Widolin, M. R., and Barbosa-Junior, A. (2005). Evaluation of rapid tests for anti-HIV detection in Brazil. *AIDS* 19 Suppl 4, S70-5.
- Fiebig, E. W., Wright, D. J., Rawal, B. D., Garrett, P. E., Schumacher, R. T., Peddada, L., Heldebrant, C., Smith, R., Conrad, A., Kleinman, S. H., and Busch, M. P. (2003). Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. *AIDS* 17(13), 1871-9.
- Fischetti, L., Opare-Sem, O., Candotti, D., Lee, H., and Allain, J. P. (2004a). Higher viral load may explain the dominance of CRF02\_AG in the molecular epidemiology of HIV in Ghana. *AIDS* 18(8), 1208-10.
- Fischetti, L., Opare-Sem, O., Candotti, D., Sarkodie, F., Lee, H., and Allain, J. P. (2004b). Molecular epidemiology of HIV in Ghana: dominance of CRF02\_AG. *J Med Virol* 73(2), 158-66.
- Flys, T. S., Chen, S., Jones, D. C., Hoover, D. R., Church, J. D., Fiscus, S. A., Mwatha, A., Guay, L. A., Mmiro, F., Musoke, P., Kumwenda, N., Taha, T. E., Jackson, J. B., and Eshleman, S. H. (2006). Quantitative analysis of HIV-1 variants with the K103N resistance mutation after single-dose nevirapine in women with HIV-1 subtypes A, C, and D. *J Acquir Immune Defic Syndr* 42(5), 610-3.
- Fontaine, E., Riva, C., Peeters, M., Schmit, J. C., Delaporte, E., Van Laethem, K., Van Vaerenbergh, K., Snoeck, J., Van Wijngaerden, E., De Clercq, E., Van Ranst, M., and Vandamme, A. M. (2001). Evaluation of two commercial kits for the detection of

- genotypic drug resistance on a panel of HIV type 1 subtypes A through J. *J Acquir Immune Defic Syndr* 28(3), 254-8.
- Fowler, M. G., and Rogers, M. F. (1996). Overview of perinatal HIV infection. *J Nutr* 126(10 Suppl), 2602S-2607S.
- Frater, A. J., Beardall, A., Ariyoshi, K., Churchill, D., Galpin, S., Clarke, J. R., Weber, J. N., and McClure, M. O. (2001). Impact of baseline polymorphisms in RT and protease on outcome of highly active antiretroviral therapy in HIV-1-infected African patients. *AIDS* 15(12), 1493-502.
- Galai, N., Kalinkovich, A., Burstein, R., Vlahov, D., and Bentwich, Z. (1997). African HIV-1 subtype C and rate of progression among Ethiopian immigrants in Israel. *Lancet* 349(9046), 180-1.
- Galimand, J., Frange, P., Rouzioux, C., Deveau, C., Avettand-Fenoel, V., Ghosn, J., Lascoux, C., Goujard, C., Meyer, L., and Chaix, M. L. (2010). Short communication: evidence of HIV type 1 complex and second generation recombinant strains among patients infected in 1997-2007 in France: ANRS CO06 PRIMO Cohort. *AIDS Res Hum Retroviruses* 26(6), 645-51.
- Gao, F., Robertson, D. L., Morrison, S. G., Hui, H., Craig, S., Decker, J., Fultz, P. N., Girard, M., Shaw, G. M., Hahn, B. H., and Sharp, P. M. (1996). The heterosexual human immunodeficiency virus type 1 epidemic in Thailand is caused by an intersubtype (A/E) recombinant of African origin. *J Virol* 70(10), 7013-29.
- Gao, F., Vidal, N., Li, Y., Trask, S. A., Chen, Y., Kostrikis, L. G., Ho, D. D., Kim, J., Oh, M. D., Choe, K., Salminen, M., Robertson, D. L., Shaw, G. M., Hahn, B. H., and Peeters, M. (2001). Evidence of two distinct subsubtypes within the HIV-1 subtype A radiation. *AIDS Res Hum Retroviruses* 17(8), 675-88.
- Garrido, C., Geretti, A. M., Zahonero, N., Booth, C., Strang, A., Soriano, V., and De Mendoza, C. (2010). Integrase variability and susceptibility to HIV integrase inhibitors: impact of subtypes, antiretroviral experience and duration of HIV infection. *J Antimicrob Chemother* 65(2), 320-6.
- Garrido, C., Roulet, V., Chueca, N., Poveda, E., Aguilera, A., Skrabal, K., Zahonero, N., Carlos, S., Garcia, F., Faudon, J. L., Soriano, V., and de Mendoza, C. (2008). Evaluation of eight different bioinformatics tools to predict viral tropism in different human immunodeficiency virus type 1 subtypes. *J Clin Microbiol* 46(3), 887-91.
- Garrido, C., Zahonero, N., Corral, A., Arredondo, M., Soriano, V., and de Mendoza, C. (2009). Correlation between human immunodeficiency virus type 1 (HIV-1) RNA measurements obtained with dried blood spots and those obtained with plasma by use of Nuclisens EasyQ HIV-1 and Abbott RealTime HIV load tests. *J Clin Microbiol* 47(4), 1031-6.
- Gaudy, C., Moreau, A., Brunet, S., Descamps, J. M., Deleplanque, P., Brand, D., and Barin, F. (2004). Subtype B human immunodeficiency virus (HIV) type 1 mutant that escapes detection in a fourth-generation immunoassay for HIV infection. *J Clin Microbiol* 42(6), 2847-9.
- Geelen, S., Lange, J., Borleffs, J., Wolfs, T., Weersink, A., and Schuurman, R. (2003). Failure to detect a non-B HIV-1 subtype by the HIV-1 Amplicor Monitor test, version 1.5: a case of unexpected vertical transmission. *AIDS* 17(5), 781-2.
- Geretti, A. M., Harrison, L., Green, H., Sabin, C., Hill, T., Fearnhill, E., Pillay, D., and Dunn, D. (2009). Effect of HIV-1 subtype on virologic and immunologic response to starting highly active antiretroviral therapy. *Clin Infect Dis* 48(9), 1296-305.

- Germer, J. J., Gerads, T. M., Mandrekar, J. N., Mitchell, P. S., and Yao, J. D. (2006). Detection of HIV-1 proviral DNA with the AMPLICOR HIV-1 DNA Test, version 1.5, following sample processing by the MagNA Pure LC instrument. *J Clin Virol* 37(3), 195-8.
- Gonzalez, L. M., Brindeiro, R. M., Aguiar, R. S., Pereira, H. S., Abreu, C. M., Soares, M. A., and Tanuri, A. (2004). Impact of nelfinavir resistance mutations on in vitro phenotype, fitness, and replication capacity of human immunodeficiency virus type 1 with subtype B and C proteases. *Antimicrob Agents Chemother* 48(9), 3552-5.
- Gonzalez, L. M., Brindeiro, R. M., Tarin, M., Calazans, A., Soares, M. A., Cassol, S., and Tanuri, A. (2003). In vitro hypersusceptibility of human immunodeficiency virus type 1 subtype C protease to lopinavir. *Antimicrob Agents Chemother* 47(9), 2817-22.
- Gonzalez, S., Gondwe, C., Tully, D. C., Minhas, V., Shea, D., Kankasa, C., M'Soka, T., and Wood, C. (2010). Short communication: antiretroviral therapy resistance mutations present in the HIV type 1 subtype C pol and env regions from therapy-naive patients in Zambia. *AIDS Res Hum Retroviruses* 26(7), 795-803.
- Gottesman, B. S., Grossman, Z., Lorber, M., Levi, I., Shitrit, P., Katzir, M., Shahar, E., Gottesman, G., and Chowers, M. (2006). Comparative performance of the Amplicor HIV-1 Monitor Assay versus NucliSens EasyQ in HIV subtype C-infected patients. *J Med Virol* 78(7), 883-7.
- Grant, P. M., and Zolopa, A. R. (2009). The use of resistance testing in the management of HIV-1-infected patients. *Curr Opin HIV AIDS* 4(6), 474-80.
- Grant, R. M., Kuritzkes, D. R., Johnson, V. A., Mellors, J. W., Sullivan, J. L., Swanstrom, R., D'Aquila, R. T., Van Gorder, M., Holodniy, M., Lloyd Jr, R. M., Jr., Reid, C., Morgan, G. F., and Winslow, D. L. (2003). Accuracy of the TRUGENE HIV-1 genotyping kit. *J Clin Microbiol* 41(4), 1586-93.
- Grossman, Z., Istomin, V., Averbuch, D., Lorber, M., Risenberg, K., Levi, I., Chowers, M., Burke, M., Bar Yaacov, N., and Schapiro, J. M. (2004). Genetic variation at NNRTI resistance-associated positions in patients infected with HIV-1 subtype C. *AIDS* 18(6), 909-15.
- Grossman, Z., Vardinon, N., Chemtob, D., Alkan, M. L., Bentwich, Z., Burke, M., Gottesman, G., Istomin, V., Levi, I., Maayan, S., Shahar, E., and Schapiro, J. M. (2001). Genotypic variation of HIV-1 reverse transcriptase and protease: comparative analysis of clade C and clade B. *AIDS* 15(12), 1453-60.
- Gupta, R. K., Chrystie, I. L., O'Shea, S., Mullen, J. E., Kulasegaram, R., and Tong, C. Y. (2005). K65R and Y181C are less prevalent in HAART-experienced HIV-1 subtype A patients. *AIDS* 19(16), 1916-9.
- Gurtler, L. G., Hauser, P. H., Eberle, J., von Brunn, A., Knapp, S., Zekeng, L., Tsague, J. M., and Kaptue, L. (1994). A new subtype of human immunodeficiency virus type 1 (MVP-5180) from Cameroon. *J Virol* 68(3), 1581-5.
- Habekova, M., Takacova, M., Lysy, J., Mokras, M., Camacho, R., Truska, P., and Stanekova, D. (2010). Genetic subtypes of HIV type 1 circulating in Slovakia. *AIDS Res Hum Retroviruses* 26(10), 1103-7.
- Harris, M. E., Serwadda, D., Sewankambo, N., Kim, B., Kigozi, G., Kiwanuka, N., Phillips, J. B., Wabwire, F., Meehen, M., Lutalo, T., Lane, J. R., Merling, R., Gray, R., Wawer, M., Birx, D. L., Robb, M. L., and McCutchan, F. E. (2002). Among 46 near full length HIV type 1 genome sequences from Rakai District, Uganda, subtype D and AD recombinants predominate. *AIDS Res Hum Retroviruses* 18(17), 1281-90.
- Hawkins, C. A., Chaplin, B., Idoko, J., Ekong, E., Adewole, I., Gashau, W., Murphy, R. L., and Kanki, P. (2009). Clinical and genotypic findings in HIV-infected patients with

- the K65R mutation failing first-line antiretroviral therapy in Nigeria. *J Acquir Immune Defic Syndr* 52(2), 228-34.
- Henquell, C., Jacomet, C., Antoniotti, O., Chaib, A., Regagnon, C., Brunet, S., Peigue-Lafeuille, H., and Barin, F. (2008). Difficulties in diagnosing group o human immunodeficiency virus type 1 acute primary infection. *J Clin Microbiol* 46(7), 2453-6.
- Herring, B. L., Ge, Y. C., Wang, B., Ratnamohan, M., Zheng, F., Cunningham, A. L., Saksena, N. K., and Dwyer, D. E. (2003). Segregation of human immunodeficiency virus type 1 subtypes by risk factor in Australia. *J Clin Microbiol* 41(10), 4600-4.
- Holguin, A., De Arellano, E. R., and Soriano, V. (2007). Amino acid conservation in the gp41 transmembrane protein and natural polymorphisms associated with enfuvirtide resistance across HIV-1 variants. *AIDS Res Hum Retroviruses* 23(9), 1067-74.
- Holguin, A., Gutierrez, M., Portocarrero, N., Rivas, P., and Baquero, M. (2009). Performance of OraQuick Advance Rapid HIV-1/2 Antibody Test for detection of antibodies in oral fluid and serum/plasma in HIV-1+ subjects carrying different HIV-1 subtypes and recombinant variants. *J Clin Virol* 45(2), 150-2.
- Holguin, A., Hertogs, K., and Soriano, V. (2003). Performance of drug resistance assays in testing HIV-1 non-B subtypes. *Clin Microbiol Infect* 9(4), 323-6.
- Holguin, A., Lopez, M., Molinero, M., and Soriano, V. (2008). Performance of three commercial viral load assays, Versant human immunodeficiency virus type 1 (HIV-1) RNA bDNA v3.0, Cobas AmpliPrep/Cobas TaqMan HIV-1, and NucliSens HIV-1 EasyQ v1.2, testing HIV-1 non-B subtypes and recombinant variants. *J Clin Microbiol* 46(9), 2918-23.
- Holguin, A., Paxinos, E., Hertogs, K., Womac, C., and Soriano, V. (2004). Impact of frequent natural polymorphisms at the protease gene on the in vitro susceptibility to protease inhibitors in HIV-1 non-B subtypes. *J Clin Virol* 31(3), 215-20.
- Hosseinipour, M. C., van Oosterhout, J. J., Weigel, R., Phiri, S., Kamwendo, D., Parkin, N., Fiscus, S. A., Nelson, J. A., Eron, J. J., and Kumwenda, J. (2009). The public health approach to identify antiretroviral therapy failure: high-level nucleoside reverse transcriptase inhibitor resistance among Malawians failing first-line antiretroviral therapy. *AIDS* 23(9), 1127-34.
- Hsu, L. Y., Subramaniam, R., Bacheler, L., and Paton, N. I. (2005). Characterization of mutations in CRF01\_AE virus isolates from antiretroviral treatment-naive and -experienced patients in Singapore. *J Acquir Immune Defic Syndr* 38(1), 5-13.
- Huang, W., Eshleman, S. H., Toma, J., Fransen, S., Stawiski, E., Paxinos, E. E., Whitcomb, J. M., Young, A. M., Donnell, D., Mmiro, F., Musoke, P., Guay, L. A., Jackson, J. B., Parkin, N. T., and Petropoulos, C. J. (2007). Coreceptor tropism in human immunodeficiency virus type 1 subtype D: high prevalence of CXCR4 tropism and heterogeneous composition of viral populations. *J Virol* 81(15), 7885-93.
- Hudgens, M. G., Longini, I. M., Jr., Vanichseni, S., Hu, D. J., Kitayaporn, D., Mock, P. A., Halloran, M. E., Satten, G. A., Choopanya, K., and Mastro, T. D. (2002). Subtype-specific transmission probabilities for human immunodeficiency virus type 1 among injecting drug users in Bangkok, Thailand. *Am J Epidemiol* 155(2), 159-68.
- Ikomey, G. M., Atashili, J., Okomo-Assoumou, M. C., Mesembe, M., and Ndumbe, P. M. (2009). Dried blood spots versus plasma for the quantification of HIV-1 RNA using the manual (PCR-ELISA) amplicor monitor HIV-1 version 1.5 assay in Yaounde, Cameroon. *J Int Assoc Physicians AIDS Care (Chic)* 8(3), 181-4.
- Jagodzinski, L. L., Cooley, J. D., Weber, M., and Michael, N. L. (2003). Performance characteristics of human immunodeficiency virus type 1 (HIV-1) genotyping

- systems in sequence-based analysis of subtypes other than HIV-1 subtype B. *J Clin Microbiol* 41(3), 998-1003.
- Janssens, W., Laukkanen, T., Salminen, M. O., Carr, J. K., Van der Auwera, G., Heyndrickx, L., van der Groen, G., and McCutchan, F. E. (2000). HIV-1 subtype H near-full length genome reference strains and analysis of subtype-H-containing inter-subtype recombinants. *AIDS* 14(11), 1533-43.
- Jayaraman, G. C., Gleeson, T., Rekart, M. L., Cook, D., Preiksaitis, J., Sidaway, F., Harmen, S., Dawood, M., Wood, M., Ratnam, S., Sandstrom, P., and Archibald, C. (2003). Prevalence and determinants of HIV-1 subtypes in Canada: enhancing routinely collected information through the Canadian HIV Strain and Drug Resistance Surveillance Program. *Can Commun Dis Rep*. 29(4), 29-36.
- Johannessen, A. (2010). Dried blood spots in HIV monitoring: applications in resource-limited settings. *Bioanalysis* 2(11), 1893-908.
- Johannessen, A., Garrido, C., Zahonero, N., Sandvik, L., Naman, E., Kivuyo, S. L., Kasubi, M. J., Gundersen, S. G., Bruun, J. N., and de Mendoza, C. (2009). Dried blood spots perform well in viral load monitoring of patients who receive antiretroviral treatment in rural Tanzania. *Clin Infect Dis* 49(6), 976-81.
- Johanson, J., Abravaya, K., Caminiti, W., Erickson, D., Flanders, R., Leckie, G., Marshall, E., Mullen, C., Ohhashi, Y., Perry, R., Ricci, J., Salituro, J., Smith, A., Tang, N., Vi, M., and Robinson, J. (2001). A new ultrasensitive assay for quantitation of HIV-1 RNA in plasma. *J Virol Methods* 95(1-2), 81-92.
- John-Stewart, G. C., Nduati, R. W., Rousseau, C. M., Mbori-Ngacha, D. A., Richardson, B. A., Rainwater, S., Panteleeff, D. D., and Overbaugh, J. (2005). Subtype C Is associated with increased vaginal shedding of HIV-1. *J Infect Dis* 192(3), 492-6.
- Johnson, J. A., Li, J. F., Morris, L., Martinson, N., Gray, G., McIntyre, J., and Heneine, W. (2005). Emergence of drug-resistant HIV-1 after intrapartum administration of single-dose nevirapine is substantially underestimated. *J Infect Dis* 192(1), 16-23.
- Jurriaans, S., Sankatsing, S. U., Prins, J. M., Schuitemaker, H., Lange, J., Van Der Kuyl, A. C., and Cornelissen, M. (2004). HIV-1 seroreversion in an HIV-1-seropositive patient treated during acute infection with highly active antiretroviral therapy and mycophenolate mofetil. *AIDS* 18(11), 1607-8.
- Kaleebu, P., Nankya, I. L., Yirrell, D. L., Shafer, L. A., Kyosiimire-Lugemwa, J., Lule, D. B., Morgan, D., Beddows, S., Weber, J., and Whitworth, J. A. (2007). Relation between chemokine receptor use, disease stage, and HIV-1 subtypes A and D: results from a rural Ugandan cohort. *J Acquir Immune Defic Syndr* 45(1), 28-33.
- Kalish, M. L., Robbins, K. E., Pieniazek, D., Schaefer, A., Nzilambi, N., Quinn, T. C., St Louis, M. E., Youngpairoj, A. S., Phillips, J., Jaffe, H. W., and Folks, T. M. (2004). Recombinant viruses and early global HIV-1 epidemic. *Emerg Infect Dis* 10(7), 1227-34.
- Kane, C. T., Ndiaye, H. D., Diallo, S., Ndiaye, I., Wade, A. S., Diaw, P. A., Gaye-Diallo, A., and Mboup, S. (2008). Quantitation of HIV-1 RNA in dried blood spots by the real-time NucliSENS EasyQ HIV-1 assay in Senegal. *J Virol Methods* 148(1-2), 291-5.
- Kantor, R., and Katzenstein, D. (2003). Polymorphism in HIV-1 non-subtype B protease and reverse transcriptase and its potential impact on drug susceptibility and drug resistance evolution. *AIDS Rev* 5(1), 25-35.
- Kantor, R., and Katzenstein, D. (2004). Drug resistance in non-subtype B HIV-1. *J Clin Virol* 29(3), 152-9.
- Katsoulidou, A., Rokka, C., Issaris, C., Haida, C., Tzannis, K., Sypsa, V., Detsika, M., Paraskevis, D., and Hatzakis, A. (2011). Comparative evaluation of the performance

- of the Abbott RealTime HIV-1 assay for measurement of HIV-1 plasma viral load on genetically diverse samples from Greece. *Virology* 8, 10.
- Keller, M., Lu, Y., Lalonde, R. G., and Klein, M. B. (2009). Impact of HIV-1 viral subtype on CD4+ T-cell decline and clinical outcomes in antiretroviral naive patients receiving universal healthcare. *AIDS* 23(6), 731-7.
- Kiwanuka, N., Laeyendecker, O., Quinn, T. C., Wawer, M. J., Shepherd, J., Robb, M., Kigozi, G., Kagaayi, J., Serwadda, D., Makumbi, F. E., Reynolds, S. J., and Gray, R. H. (2009). HIV-1 subtypes and differences in heterosexual HIV transmission among HIV-discordant couples in Rakai, Uganda. *AIDS* 23(18), 2479-84.
- Kiwanuka, N., Robb, M., Laeyendecker, O., Kigozi, G., Wabwire-Mangen, F., Makumbi, F. E., Nalugoda, F., Kagaayi, J., Eller, M., Eller, L. A., Serwadda, D., Sewankambo, N. K., Reynolds, S. J., Quinn, T. C., Gray, R. H., Wawer, M. J., and Whalen, C. C. (2010). HIV-1 viral subtype differences in the rate of CD4+ T-cell decline among HIV seroincident antiretroviral naive persons in Rakai district, Uganda. *J Acquir Immune Defic Syndr* 54(2), 180-4.
- Kline, N. E., Schwarzwald, H., and Kline, M. W. (2002). False negative DNA polymerase chain reaction in an infant with subtype C human immunodeficiency virus 1 infection. *Pediatr Infect Dis J* 21(9), 885-6.
- Kong, X., West, J. T., Zhang, H., Shea, D. M., M'Soka T, J., and Wood, C. (2008). The human immunodeficiency virus type 1 envelope confers higher rates of replicative fitness to perinatally transmitted viruses than to nontransmitted viruses. *J Virol* 82(23), 11609-18.
- Korenromp, E. L., Williams, B. G., Schmid, G. P., and Dye, C. (2009). Clinical prognostic value of RNA viral load and CD4 cell counts during untreated HIV-1 infection--a quantitative review. *PLoS One* 4(6), e5950.
- Kousiappa, I., Van De Vijver, D. A., and Kostrikis, L. G. (2009). Near full-length genetic analysis of HIV sequences derived from Cyprus: evidence of a highly polyphyletic and evolving infection. *AIDS Res Hum Retroviruses* 25(8), 727-40.
- Kuritzkes, D. R. (2008). HIV-1 subtype as a determinant of disease progression. *J Infect Dis* 197(5), 638-9.
- Kwok, S., Kellogg, D. E., McKinney, N., Spasic, D., Goda, L., Levenson, C., and Sninsky, J. J. (1990). Effects of primer-template mismatches on the polymerase chain reaction: human immunodeficiency virus type 1 model studies. *Nucleic Acids Res* 18(4), 999-1005.
- Kwon, J. A., Yoon, S. Y., Lee, C. K., Lim, C. S., Lee, K. N., Sung, H. J., Brennan, C. A., and Devare, S. G. (2006). Performance evaluation of three automated human immunodeficiency virus antigen-antibody combination immunoassays. *J Virol Methods* 133(1), 20-6.
- Laforgerie, E., Boucher, B., Ly, T. D., Maisoneuve, L., Izopet, J., Delaugerre, C., and Simon, F. (2010). Sensitivity of 8 CE (European Community)-approved rapid disposable tests for anti-HIV antibody detection during and after seroconversion. *J Virol Methods* 165(1), 105-7.
- Lahuerta, M., Aparicio, E., Bardaji, A., Marco, S., Sacarlal, J., Mandomando, I., Alonso, P., Martinez, M. A., Menendez, C., and Nanche, D. (2008). Rapid spread and genetic diversification of HIV type 1 subtype C in a rural area of southern Mozambique. *AIDS Res Hum Retroviruses* 24(2), 327-35.
- Lai, A., Riva, C., Marconi, A., Balestrieri, M., Razzolini, F., Meini, G., Vicenti, I., Rosi, A., Saladini, F., Caramma, I., Franzetti, M., Rossini, V., Galli, A., Galli, M., Violin, M.,

- Zazzi, M., and Balotta, C. (2010). Changing patterns in HIV-1 non-B clade prevalence and diversity in Italy over three decades. *HIV Med* 11(9), 593-602.
- Lau, K. A., Wang, B., Miranda-Saksena, M., Boadle, R., Kamarulzaman, A., Ng, K. P., and Saksena, N. K. (2010). Evidence for possible biological advantages of the newly emerging HIV-1 circulating recombinant form from Malaysia - CRF33\_01B in comparison to its progenitors - CRF01\_AE and subtype B. *Curr HIV Res* 8(3), 259-71.
- Laukkanen, T., Carr, J. K., Janssens, W., Liitsola, K., Gotte, D., McCutchan, F. E., Op de Coul, E., Cornelissen, M., Heyndrickx, L., van der Groen, G., and Salminen, M. O. (2000). Virtually full-length subtype F and F/D recombinant HIV-1 from Africa and South America. *Virology* 269(1), 95-104.
- Laurent, C., Bourgeois, A., Faye, M. A., Mougnotou, R., Seydi, M., Gueye, M., Liegeois, F., Kane, C. T., Butel, C., Mbuagbaw, J., Zekeng, L., Mboup, S., Mpoudi-Ngole, E., Peeters, M., and Delaporte, E. (2002). No difference in clinical progression between patients infected with the predominant human immunodeficiency virus type 1 circulating recombinant form (CRF) 02\_AG strain and patients not infected with CRF02\_AG, in Western and West-Central Africa: a four-year prospective multicenter study. *J Infect Dis* 186(4), 486-92.
- Lemey, P., Pybus, O. G., Rambaut, A., Drummond, A. J., Robertson, D. L., Roques, P., Worobey, M., and Vandamme, A. M. (2004). The molecular population genetics of HIV-1 group O. *Genetics* 167(3), 1059-68.
- Leoz, M., Depatureaux, A., Vessiere, A., Roquebert, B., Damond, F., Rousset, D., Roques, P., Simon, F., and Plantier, J. C. (2008). Integrase polymorphism and HIV-1 group O diversity. *AIDS* 22(10), 1239-43.
- Li, Y., Tee, K. K., Liao, H., Hase, S., Uenishi, R., Li, X. J., Tsuchiura, T., Yang, R., Govindasamy, S., Yong, Y. K., Tan, H. Y., Pybus, O. G., Kamarulzaman, A., and Takebe, Y. (2010). Identification of a novel second-generation circulating recombinant form (CRF48\_01B) in Malaysia: a descendant of the previously identified CRF33\_01B. *J Acquir Immune Defic Syndr* 54(2), 129-36.
- Lisovsky, I., Schader, S. M., Martinez-Cajas, J. L., Oliveira, M., Moisi, D., and Wainberg, M. A. (2010). HIV-1 protease codon 36 polymorphisms and differential development of resistance to nelfinavir, lopinavir, and atazanavir in different HIV-1 subtypes. *Antimicrob Agents Chemother* 54(7), 2878-85.
- Loemba, H., Brenner, B., Parniak, M. A., Ma'ayan, S., Spira, B., Moisi, D., Oliveira, M., Detorio, M., and Wainberg, M. A. (2002). Genetic divergence of human immunodeficiency virus type 1 Ethiopian clade C reverse transcriptase (RT) and rapid development of resistance against nonnucleoside inhibitors of RT. *Antimicrob Agents Chemother* 46(7), 2087-94.
- Lofgren, S. M., Morrissey, A. B., Chevallier, C. C., Malabeja, A. I., Edmonds, S., Amos, B., Sifuna, D. J., von Seidlein, L., Schimana, W., Stevens, W. S., Bartlett, J. A., and Crump, J. A. (2009). Evaluation of a dried blood spot HIV-1 RNA program for early infant diagnosis and viral load monitoring at rural and remote healthcare facilities. *AIDS* 23(18), 2459-66.
- Los Alamos Sequence Database (2011). Los Alamos, New Mexico: Los Alamos National Laboratory <http://www.hiv.lanl.gov/>
- Loussert-Ajaka, I., Ly, T. D., Chaix, M. L., Ingrand, D., Saragosti, S., Courouce, A. M., Brun-Vezinet, F., and Simon, F. (1994). HIV-1/HIV-2 seronegativity in HIV-1 subtype O infected patients. *Lancet* 343(8910), 1393-4.



- Ly, N., Recordon-Pinson, P., Phoung, V., Srey, C., Kruey, L. S., Koum, K., Chhum, V., Glaziou, P., Fleury, H. J., and Reynes, J. M. (2005). Characterization of mutations in HIV type 1 isolates from 144 Cambodian recently infected patients and pregnant women naive to antiretroviral drugs. *AIDS Res Hum Retroviruses* 21(11), 971-6.
- Ly, T. D., Ebel, A., Faucher, V., Fihman, V., and Laperche, S. (2007). Could the new HIV combined p24 antigen and antibody assays replace p24 antigen specific assays? *J Virol Methods* 143(1), 86-94.
- Ly, T. D., Laperche, S., Brennan, C., Vallari, A., Ebel, A., Hunt, J., Martin, L., Daghfal, D., Schochetman, G., and Devare, S. (2004). Evaluation of the sensitivity and specificity of six HIV combined p24 antigen and antibody assays. *J Virol Methods* 122(2), 185-94.
- Ly, T. D., Martin, L., Daghfal, D., Sandridge, A., West, D., Bristow, R., Chalouas, L., Qiu, X., Lou, S. C., Hunt, J. C., Schochetman, G., and Devare, S. G. (2001). Seven human immunodeficiency virus (HIV) antigen-antibody combination assays: evaluation of HIV seroconversion sensitivity and subtype detection. *J Clin Microbiol* 39(9), 3122-8.
- MacDonald, K. S., Embree, J., Njenga, S., Nagelkerke, N. J., Ngatia, I., Mohammed, Z., Barber, B. H., Ndinya-Achola, J., Bwayo, J., and Plummer, F. A. (1998). Mother-child class I HLA concordance increases perinatal human immunodeficiency virus type 1 transmission. *J Infect Dis* 177(3), 551-6.
- Maes, B., Schrooten, Y., Snoeck, J., Derdelinckx, I., Van Ranst, M., Vandamme, A. M., and Van Laethem, K. (2004). Performance of ViroSeq HIV-1 Genotyping System in routine practice at a Belgian clinical laboratory. *J Virol Methods* 119(1), 45-9.
- Magiorkinis, G., Paraskevis, D., Magiorkinis, E., Vandamme, A. M., and Hatzakis, A. (2002). Reanalysis of the HIV-1 circulating recombinant form A/E (CRF01\_AE): evidence of A/E/G recombination. *J Acquir Immune Defic Syndr* 30(1), 124-9.
- Maiga, A. I., Descamps, D., Morand-Joubert, L., Malet, I., Derache, A., Cisse, M., Koita, V., Akonde, A., Diarra, B., Wiriden, M., Tounkara, A., Verlinden, Y., Katlama, C., Costagliola, D., Masquelier, B., Calvez, V., and Marcelin, A. G. (2010). Resistance-associated mutations to etravirine (TMC-125) in antiretroviral-naive patients infected with non-B HIV-1 subtypes. *Antimicrob Agents Chemother* 54(2), 728-33.
- Makuwa, M., Souquiere, S., Niangui, M. T., Rouquet, P., Apetrei, C., Roques, P., and Simon, F. (2002). Reliability of rapid diagnostic tests for HIV variant infection. *J Virol Methods* 103(2), 183-90.
- Maljkovic, I., Wilbe, K., Solver, E., Alaeus, A., and Leitner, T. (2003). Limited transmission of drug-resistant HIV type 1 in 100 Swedish newly detected and drug-naive patients infected with subtypes A, B, C, D, G, U, and CRF01\_AE. *AIDS Res Hum Retroviruses* 19(11), 989-97.
- Mamadou, S., Vidal, N., Montavon, C., Ben, A., Djibo, A., Rabiou, S., Soga, G., Delaporte, E., Mboup, S., and Peeters, M. (2003). Emergence of complex and diverse CRF02-AG/CRF06-cpx recombinant HIV type 1 strains in Niger, West Africa. *AIDS Res Hum Retroviruses* 19(1), 77-82.
- Marconi, V. C., Sunpath, H., Lu, Z., Gordon, M., Koranteng-Apeagyei, K., Hampton, J., Carpenter, S., Giddy, J., Ross, D., Holst, H., Losina, E., Walker, B. D., and Kuritzkes, D. R. (2008). Prevalence of HIV-1 drug resistance after failure of a first highly active antiretroviral therapy regimen in KwaZulu Natal, South Africa. *Clin Infect Dis* 46(10), 1589-97.
- Marechal, V., Jauvin, V., Selekon, B., Leal, J., Pelembi, P., Fikouma, V., Gabrie, P., Heredeibona, L. S., Goumba, C., Serdouma, E., Ayouba, A., and Fleury, H. (2006). Increasing HIV type 1 polymorphic diversity but no resistance to antiretroviral

- drugs in untreated patients from Central African Republic: a 2005 study. *AIDS Res Hum Retroviruses* 22(10), 1036-44.
- Martinez-Cajas, J. L., Pant-Pai, N., Klein, M. B., and Wainberg, M. A. (2008). Role of genetic diversity amongst HIV-1 non-B subtypes in drug resistance: a systematic review of virologic and biochemical evidence. *AIDS Rev* 10(4), 212-23.
- Martinez, A. M., Hora, V. P., Santos, A. L., Mendoza-Sassi, R., Von Groll, A., Soares, E. A., D'Avila, N., Silveira, J., Leal, R. G., Tanuri, A., and Soares, M. A. (2006). Determinants of HIV-1 mother-to-child transmission in Southern Brazil. *An Acad Bras Cienc* 78(1), 113-21.
- Mbida, A. D., Sosso, S., Flori, P., Saoudin, H., Lawrence, P., Monny-Lobe, M., Oyono, Y., Ndzi, E., Cappelli, G., Lucht, F., Pozzetto, B., Oukem-Boyer, O. O., and Bourlet, T. (2009). Measure of viral load by using the Abbott Real-Time HIV-1 assay on dried blood and plasma spot specimens collected in 2 rural dispensaries in Cameroon. *J Acquir Immune Defic Syndr* 52(1), 9-16.
- McCutchan, F. E. (2006). Global epidemiology of HIV. *J Med Virol* 78 Suppl 1, S7-S12.
- McGowan, J. P., and Shah, S. S. (2000). Prevention of perinatal HIV transmission during pregnancy. *J Antimicrob Chemother* 46(5), 657-68.
- Mellors, J. W., Munoz, A., Giorgi, J. V., Margolick, J. B., Tassoni, C. J., Gupta, P., Kingsley, L. A., Todd, J. A., Saah, A. J., Detels, R., Phair, J. P., and Rinaldo, C. R., Jr. (1997). Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. *Ann Intern Med* 126(12), 946-54.
- Meloni, S. T., Kim, B., Sankale, J. L., Hamel, D. J., Tovanabutra, S., Mboup, S., McCutchan, F. E., and Kanki, P. J. (2004). Distinct human immunodeficiency virus type 1 subtype A virus circulating in West Africa: sub-subtype A3. *J Virol* 78(22), 12438-45.
- Miller, M. D., Margot, N., McColl, D., and Cheng, A. K. (2007). K65R development among subtype C HIV-1-infected patients in tenofovir DF clinical trials. *AIDS* 21(2), 265-6.
- Mintsa-Ndong, A., Caron, M., Plantier, J. C., Makuwa, M., Le Hello, S., Courgnaud, V., Roques, P., and Kazanji, M. (2009). High HIV Type 1 prevalence and wide genetic diversity with dominance of recombinant strains but low level of antiretroviral drug-resistance mutations in untreated patients in northeast Gabon, Central Africa. *AIDS Res Hum Retroviruses* 25(4), 411-8.
- Mokili, J. L., Wade, C. M., Burns, S. M., Cutting, W. A., Bopopi, J. M., Green, S. D., Peutherer, J. F., and Simmonds, P. (1999). Genetic heterogeneity of HIV type 1 subtypes in Kimpese, rural Democratic Republic of Congo. *AIDS Res Hum Retroviruses* 15(7), 655-64.
- Montavon, C., Vergne, L., Bourgeois, A., Mpoudi-Ngole, E., Malonga-Mouellet, G., Butel, C., Toure-Kane, C., Delaporte, E., and Peeters, M. (2002). Identification of a new circulating recombinant form of HIV type 1, CRF11-cpx, involving subtypes A, G, J, and CRF01-AE, in Central Africa. *AIDS Res Hum Retroviruses* 18(3), 231-6.
- Monteiro-Cunha, J. P., Araujo, A. F., Santos, E., Galvao-Castro, B., and Alcantara, L. C. (2011). Lack of high-level resistance mutations in HIV type 1 BF recombinant strains circulating in northeast Brazil. *AIDS Res Hum Retroviruses* 27(6), 623-31.
- Morison, L., Buve, A., Zekeng, L., Heyndrickx, L., Anagonou, S., Musonda, R., Kahindo, M., Weiss, H. A., Hayes, R. J., Laga, M., Janssens, W., and van der Groen, G. (2001). HIV-1 subtypes and the HIV epidemics in four cities in sub-Saharan Africa. *AIDS* 15 Suppl 4, S109-16.
- Munerato, P., Sucupira, M. C., Oliveros, M. P., Janini, L. M., de Souza, D. F., Pereira, A. A., Inocencio, L. A., and Diaz, R. S. (2010). HIV type 1 antiretroviral resistance

- mutations in subtypes B, C, and F in the City of Sao Paulo, Brazil. *AIDS Res Hum Retroviruses* 26(3), 265-73.
- Murray, M. C., Embree, J. E., Ramdahin, S. G., Anzala, A. O., Njenga, S., and Plummer, F. A. (2000). Effect of human immunodeficiency virus (HIV) type 1 viral genotype on mother-to-child transmission of HIV-1. *J Infect Dis* 181(2), 746-9.
- Neogi, U., Sood, V., Banerjee, S., Ghosh, N., Verma, S., Samrat, S., Sharma, Y., Saxena, A., Husain, S., Ramachandran, V. G., Das, S., Sreedhar, K. V., Goel, N., Wanchu, A., and Banerjee, A. C. (2009a). Global HIV-1 molecular epidemiology with special reference to genetic analysis of HIV-1 subtypes circulating in North India: functional and pathogenic implications of genetic variation. *Indian J Exp Biol* 47(6), 424-31.
- Neogi, U., Sood, V., Chowdhury, A., Das, S., Ramachandran, V. G., Sreedhar, V. K., Wanchu, A., Ghosh, N., and Banerjee, A. C. (2009b). Genetic analysis of HIV-1 Circulating Recombinant Form 02\_AG, B and C subtype-specific envelope sequences from Northern India and their predicted co-receptor usage. *AIDS Res Ther* 6, 28.
- (2010). DIAGNOSIS OF PEDIATRIC HIV INFECTION IN HIV-EXPOSED INFANTS. [www.hivguidelines.org](http://www.hivguidelines.org) New York State Department of Health AIDS Institute.
- Nicastri, E., Sarmati, L., d'Ettoire, G., Parisi, S. G., Palmisano, L., Montano, M., Buonomini, A. R., Galluzzo, C., Vullo, V., Concia, E., Vella, S., and Andreoni, M. (2004). Non-B HIV type 1 subtypes: replicative capacity and response to antiretroviral therapy. *AIDS Res Hum Retroviruses* 20(8), 816-8.
- Nkengafac, A., Tina, S., Sua, F., Mason, T., Auyuketta, N., and Oben, S. (2007). *XVI Drug Resistance Workshop: Basic Principles and Clinical Implications*.
- Obaro, S. K., Losikoff, P., Harwell, J., and Pugatch, D. (2005). Failure of serial human immunodeficiency virus type 1 DNA polymerase chain reactions to identify human immunodeficiency virus type 1 clade A/G. *Pediatr Infect Dis J* 24(2), 183-4.
- Oliveira, V., Bártolo, I., Borrego, P., Rocha, C., Valadas, E., Barreto, J., Almeida, E., Antunes, F., and Taveira, N. (2011). Genetic diversity and drug resistance profiles in HIV-1 and HIV-2 infected patients from Cape Verde Islands. *AIDS Research & Human Retroviruses*, *accepted*.
- Orrell, C., Walensky, R. P., Losina, E., Pitt, J., Freedberg, K. A., and Wood, R. (2009). HIV type-1 clade C resistance genotypes in treatment-naive patients and after first virological failure in a large community antiretroviral therapy programme. *Antivir Ther* 14(4), 523-31.
- Palma, A. C., Araujo, F., Duque, V., Borges, F., Paixao, M. T., and Camacho, R. (2007). Molecular epidemiology and prevalence of drug resistance-associated mutations in newly diagnosed HIV-1 patients in Portugal. *Infect Genet Evol* 7(3), 391-8.
- Papathanasopoulos, M. A., Vardas, E., Wallis, C., Glashoff, R., Butto, S., Poli, G., Malnati, M., Clerici, M., and Ensoli, B. (2010). Characterization of HIV type 1 genetic diversity among South African participants enrolled in the AIDS Vaccine Integrated Project (AVIP) study. *AIDS Res Hum Retroviruses* 26(6), 705-9.
- Paraschiv, S., Foley, B., and Otelea, D. (2011). Diversity of HIV-1 subtype C strains isolated in Romania. *Infect Genet Evol* 11(2), 270-5.
- Paraskevis, D., Magiorkinis, E., Katsoulidou, A., Hatzitheodorou, E., Antoniadou, A., Papadopoulos, A., Poulakou, G., Pappas, V., Botsi, C., Stavrianeas, N., Lelekis, M., Chini, M., Gargalianos, P., Magafas, N., Lazanas, M., Chryssos, G., Petrikos, G., Panos, G., Kordosis, T., Theodoridou, M., Sypsa, V., and Hatzakis, A. (2005).

- Prevalence of resistance-associated mutations in newly diagnosed HIV-1 patients in Greece. *Virus Res* 112(1-2), 115-22.
- Paraskevis, D., Magiorkinis, M., Pappas, V., Pavlakis, G. N., and Hatzakis, A. (2000). Molecular characterization of a recombinant HIV type 1 isolate (A/G/E/?): unidentified regions may be derived from parental subtype E sequences. *AIDS Res Hum Retroviruses* 16(9), 845-55.
- Parczewski, M., Leszczyszyn-Pynka, M., Bander, D., Urbanska, A., Stanczak, G., and Boron-Kaczmarek, A. (2010). Characteristics of HIV-1 non-B subtype infections in Northwest Poland. *J Med Virol* 82(8), 1306-13.
- Patton, J. C., Akkers, E., Coovadia, A. H., Meyers, T. M., Stevens, W. S., and Sherman, G. G. (2007). Evaluation of dried whole blood spots obtained by heel or finger stick as an alternative to venous blood for diagnosis of human immunodeficiency virus type 1 infection in vertically exposed infants in the routine diagnostic laboratory. *Clin Vaccine Immunol* 14(2), 201-3.
- Pavie, J., Rachline, A., Loze, B., Niedbalski, L., Delaugerre, C., Laforgerie, E., Plantier, J. C., Rozenbaum, W., Chevret, S., Molina, J. M., and Simon, F. (2010). Sensitivity of five rapid HIV tests on oral fluid or finger-stick whole blood: a real-time comparison in a healthcare setting. *PLoS One* 5(7), e11581.
- Peeters, M., Gueye, A., Mboup, S., Bibollet-Ruche, F., Ekaza, E., Mulanga, C., Ouedrago, R., Gandji, R., Mpele, P., Dibanga, G., Koumare, B., Saidou, M., Esu-Williams, E., Lombart, J. P., Badombena, W., Luo, N., Vanden Haesevelde, M., and Delaporte, E. (1997). Geographical distribution of HIV-1 group O viruses in Africa. *AIDS* 11(4), 493-8.
- Pereyra, F., Jia, X., McLaren, P. J., Telenti, A., de Bakker, P. I., Walker, B. D., Ripke, S., Brumme, C. J., Pulit, S. L., Carrington, M., Kadie, C. M., Carlson, J. M., Heckerman, D., Graham, R. R., Plenge, R. M., Deeks, S. G., Gianniny, L., Crawford, G., Sullivan, J., Gonzalez, E., Davies, L., Camargo, A., Moore, J. M., Beattie, N., Gupta, S., Crenshaw, A., Burt, N. P., Guiducci, C., Gupta, N., Gao, X., Qi, Y., Yuki, Y., Piechocka-Trocha, A., Cutrell, E., Rosenberg, R., Moss, K. L., Lemay, P., O'Leary, J., Schaefer, T., Verma, P., Toth, I., Block, B., Baker, B., Rothchild, A., Lian, J., Proudfoot, J., Alvino, D. M., Vine, S., Addo, M. M., Allen, T. M., Altfeld, M., Henn, M. R., Le Gall, S., Streeck, H., Haas, D. W., Kuritzkes, D. R., Robbins, G. K., Shafer, R. W., Gulick, R. M., Shikuma, C. M., Haubrich, R., Riddler, S., Sax, P. E., Daar, E. S., Ribaud, H. J., Agan, B., Agarwal, S., Ahern, R. L., Allen, B. L., Altidor, S., Altschuler, E. L., Ambardar, S., Anastos, K., Anderson, B., Anderson, V., Andrady, U., Antoniskis, D., Bangsberg, D., Barbaro, D., Barrie, W., Bartczak, J., Barton, S., Basden, P., Basgoz, N., Bazner, S., Bellos, N. C., Benson, A. M., Berger, J., Bernard, N. F., Bernard, A. M., Birch, C., Bodner, S. J., Bolan, R. K., Boudreaux, E. T., Bradley, M., Braun, J. F., Brndjar, J. E., Brown, S. J., Brown, K., Brown, S. T., Burack, J., Bush, L. M., Cafaro, V., Campbell, O., Campbell, J., Carlson, R. H., Carmichael, J. K., Casey, K. K., Cavacuiti, C., Celestin, G., Chambers, S. T., Chez, N., Chirch, L. M., Cimoch, P. J., Cohen, D., Cohn, L. E., Conway, B., Cooper, D. A., Cornelson, B., Cox, D. T., Cristofano, M. V., Cuchural, G., Jr., Czartoski, J. L., Dahman, J. M., Daly, J. S., Davis, B. T., Davis, K., Davod, S. M., DeJesus, E., Dietz, C. A., Dunham, E., Dunn, M. E., Ellerin, T. B., Eron, J. J., Fangman, J. J., Farel, C. E., Ferlazzo, H., Fidler, S., Fleenor-Ford, A., Frankel, R., Freedberg, K. A., French, N. K., Fuchs, J. D., Fuller, J. D., Gaberman, J., Gallant, J. E., Gandhi, R. T., Garcia, E., Garmon, D., Gathe, J. C., Jr., Gaultier, C. R., Gebre, W., Gilman, F. D., Gilson, I., Goepfert, P. A., Gottlieb, M. S., Goulston, C., Groger, R. K., Gurley, T. D., Haber, S., Hardwicke, R., Hardy, W.

- D., Harrigan, P. R., Hawkins, T. N., Heath, S., Hecht, F. M., Henry, W. K., Hladek, M., Hoffman, R. P., Horton, J. M., Hsu, R. K., Huhn, G. D., Hunt, P., Hupert, M. J., Illeman, M. L., Jaeger, H., Jellinger, R. M., John, M., Johnson, J. A., Johnson, K. L., Johnson, H., Johnson, K., Joly, J., Jordan, W. C., Kauffman, C. A., Khanlou, H., Killian, R. K., Kim, A. Y., Kim, D. D., Kinder, C. A., Kirchner, J. T., Kogelman, L., Kojic, E. M., Korhuis, P. T., Kurisu, W., Kwon, D. S., LaMar, M., Lampiris, H., Lanzafame, M., Lederman, M. M., Lee, D. M., Lee, J. M., Lee, M. J., Lee, E. T., Lemoine, J., Levy, J. A., Llibre, J. M., Liguori, M. A., Little, S. J., Liu, A. Y., Lopez, A. J., Loutfy, M. R., Loy, D., Mohammed, D. Y., Man, A., Mansour, M. K., Marconi, V. C., Markowitz, M., Marques, R., Martin, J. N., Martin, H. L., Jr., Mayer, K. H., McElrath, M. J., McGhee, T. A., McGovern, B. H., McGowan, K., McIntyre, D., McLeod, G. X., Menezes, P., Mesa, G., Metroka, C. E., Meyer-Olson, D., Miller, A. O., Montgomery, K., Mounzer, K. C., Nagami, E. H., Nagin, I., Nahass, R. G., Nelson, M. O., Nielsen, C., Norene, D. L., O'Connor, D. H., Ojikutu, B. O., Okulicz, J., Oladehin, O. O., Oldfield, E. C., 3rd, Olender, S. A., Ostrowski, M., Owen, W. F., Jr., Pae, E., Parsonnet, J., Pavlatos, A. M., Perlmutter, A. M., Pierce, M. N., Pincus, J. M., Pisani, L., Price, L. J., Proia, L., Prokesch, R. C., Pujet, H. C., Ramgopal, M., Rathod, A., Rausch, M., Ravishankar, J., Rhame, F. S., Richards, C. S., Richman, D. D., Rodes, B., Rodriguez, M., Rose, R. C., 3rd, Rosenberg, E. S., Rosenthal, D., Ross, P. E., Rubin, D. S., Rumbaugh, E., Saenz, L., Salvaggio, M. R., Sanchez, W. C., Sanjana, V. M., Santiago, S., Schmidt, W., Schuitemaker, H., Sestak, P. M., Shalit, P., Shay, W., Shirvani, V. N., Silebi, V. I., Sizemore, J. M., Jr., Skolnik, P. R., Sokol-Anderson, M., Sosman, J. M., Stabile, P., Stapleton, J. T., Starrett, S., Stein, F., Stellbrink, H. J., Serman, F. L., Stone, V. E., Stone, D. R., Tambussi, G., Taplitz, R. A., Tedaldi, E. M., Theisen, W., Torres, R., Tosiello, L., Tremblay, C., Tribble, M. A., Trinh, P. D., Tsao, A., Ueda, P., Vaccaro, A., Valadas, E., Vanig, T. J., Vecino, I., Vega, V. M., Veikley, W., Wade, B. H., Walworth, C., Wanidworanun, C., Ward, D. J., Warner, D. A., Weber, R. D., Webster, D., Weis, S., Wheeler, D. A., White, D. J., Wilkins, E., Winston, A., Wlodaver, C. G., van't Wout, A., Wright, D. P., Yang, O. O., Yurdin, D. L., Zabukovic, B. W., Zachary, K. C., Zeeman, B., and Zhao, M. (2010). The major genetic determinants of HIV-1 control affect HLA class I peptide presentation. *Science* 330(6010), 1551-7.
- Perez-Alvarez, L., Munoz, M., Delgado, E., Miralles, C., Ocampo, A., Garcia, V., Thomson, M., Contreras, G., and Najera, R. (2006). Isolation and biological characterization of HIV-1 BG intersubtype recombinants and other genetic forms circulating in Galicia, Spain. *J Med Virol* 78(12), 1520-8.
- Pillay, D., Walker, A. S., Gibb, D. M., de Rossi, A., Kaye, S., Ait-Khaled, M., Munoz-Fernandez, M., and Babiker, A. (2002). Impact of human immunodeficiency virus type 1 subtypes on virologic response and emergence of drug resistance among children in the Paediatric European Network for Treatment of AIDS (PENTA) 5 trial. *J Infect Dis* 186(5), 617-25.
- Ping, L. H., Nelson, J. A., Hoffman, I. F., Schock, J., Lamers, S. L., Goodman, M., Vernazza, P., Kazembe, P., Maida, M., Zimba, D., Goodenow, M. M., Eron, J. J., Jr., Fiscus, S. A., Cohen, M. S., and Swanstrom, R. (1999). Characterization of V3 sequence heterogeneity in subtype C human immunodeficiency virus type 1 isolates from Malawi: underrepresentation of X4 variants. *J Virol* 73(8), 6271-81.
- Plantier, J. C., Djemai, M., Lemeé, V., Reggiani, A., Leoz, M., Burc, L., Vessiere, A., Rousset, D., Poveda, J. D., Henquell, C., Gautheret-Dejean, A., and Barin, F. (2009a). Census

- and analysis of persistent false-negative results in serological diagnosis of human immunodeficiency virus type 1 group O infections. *J Clin Microbiol* 47(9), 2906-11.
- Plantier, J. C., Leoz, M., Dickerson, J. E., De Oliveira, F., Cordonnier, F., Lemee, V., Damond, F., Robertson, D. L., and Simon, F. (2009b). A new human immunodeficiency virus derived from gorillas. *Nat Med* 15(8), 871-2.
- Plate, D. K. (2007). Evaluation and implementation of rapid HIV tests: the experience in 11 African countries. *AIDS Res Hum Retroviruses* 23(12), 1491-8.
- Poveda, E., de Mendoza, C., Martin-Carbonero, L., Corral, A., Briz, V., Gonzalez-Lahoz, J., and Soriano, V. (2007). Prevalence of darunavir resistance mutations in HIV-1-infected patients failing other protease inhibitors. *J Antimicrob Chemother* 60(4), 885-8.
- Poveda, E., Rodes, B., Toro, C., and Soriano, V. (2004). Are fusion inhibitors active against all HIV variants? *AIDS Res Hum Retroviruses* 20(3), 347-8.
- Powell, R. L., Zhao, J., Konings, F. A., Tang, S., Ewane, L., Burda, S., Urbanski, M. M., Saa, D. R., Hewlett, I., and Nyambi, P. N. (2007a). Circulating recombinant form (CRF) 37\_cpx: an old strain in Cameroon composed of diverse, genetically distant lineages of subtypes A and G. *AIDS Res Hum Retroviruses* 23(7), 923-33.
- Powell, R. L., Zhao, J., Konings, F. A., Tang, S., Nanfack, A., Burda, S., Urbanski, M. M., Saa, D. R., Hewlett, I., and Nyambi, P. N. (2007b). Identification of a novel circulating recombinant form (CRF) 36\_cpx in Cameroon that combines two CRFs (01\_AE and 02\_AG) with ancestral lineages of subtypes A and G. *AIDS Res Hum Retroviruses* 23(8), 1008-19.
- Rajesh, L., Karunaianantham, R., Narayanan, P. R., and Swaminathan, S. (2009). Antiretroviral drug-resistant mutations at baseline and at time of failure of antiretroviral therapy in HIV type 1-coinfected TB patients. *AIDS Res Hum Retroviruses* 25(11), 1179-85.
- Raymond, S., Delobel, P., Mavigner, M., Cazabat, M., Souyris, C., Encinas, S., Sandres-Saune, K., Pasquier, C., Marchou, B., Massip, P., and Izopet, J. (2009). Genotypic prediction of human immunodeficiency virus type 1 CRF02-AG tropism. *J Clin Microbiol* 47(7), 2292-4.
- Raymond, S., Delobel, P., Mavigner, M., Cazabat, M., Souyris, C., Sandres-Saune, K., Cuzin, L., Marchou, B., Massip, P., and Izopet, J. (2008). Correlation between genotypic predictions based on V3 sequences and phenotypic determination of HIV-1 tropism. *AIDS* 22(14), F11-6.
- Raymond, S., Delobel, P., Mavigner, M., Ferradini, L., Cazabat, M., Souyris, C., Sandres-Saune, K., Pasquier, C., Marchou, B., Massip, P., and Izopet, J. (2010). Prediction of HIV type 1 subtype C tropism by genotypic algorithms built from subtype B viruses. *J Acquir Immune Defic Syndr* 53(2), 167-75.
- Read, J. S. (2007). Diagnosis of HIV-1 infection in children younger than 18 months in the United States. *Pediatrics* 120(6), e1547-62.
- Recordon-Pinson, P., Soulie, C., Flandre, P., Descamps, D., Lazrek, M., Charpentier, C., Montes, B., Trabaud, M. A., Cottalorda, J., Schneider, V., Morand-Joubert, L., Tamalet, C., Desbois, D., Mace, M., Ferre, V., Vabret, A., Ruffault, A., Pallier, C., Raymond, S., Izopet, J., Reynes, J., Marcelin, A. G., and Masquelier, B. (2010). Evaluation of the genotypic prediction of HIV-1 coreceptor use versus a phenotypic assay and correlation with the virological response to maraviroc: the ANRS GenoTropism study. *Antimicrob Agents Chemother* 54(8), 3335-40.
- Renjifo, B., Fawzi, W., Mwakagile, D., Hunter, D., Msamanga, G., Spiegelman, D., Garland, M., Kagoma, C., Kim, A., Chaplin, B., Hertzmark, E., and Essex, M. (2001).

- Differences in perinatal transmission among human immunodeficiency virus type 1 genotypes. *J Hum Virol* 4(1), 16-25.
- Renjifo, B., Gilbert, P., Chaplin, B., Msamanga, G., Mwakagile, D., Fawzi, W., and Essex, M. (2004). Preferential in-utero transmission of HIV-1 subtype C as compared to HIV-1 subtype A or D. *AIDS* 18(12), 1629-36.
- Roche Diagnostics Instruction manual, Amplicor HIV-1 DNA test, version 1.5. Singapore.
- Ross, L., Boulme, R., Fisher, R., Hernandez, J., Florance, A., Schmit, J. C., and Williams, V. (2005). A direct comparison of drug susceptibility to HIV type 1 from antiretroviral experienced subjects as assessed by the antivirogram and PhenoSense assays and by seven resistance algorithms. *AIDS Res Hum Retroviruses* 21(11), 933-9.
- Roudinskii, N. I., Sukhanova, A. L., Kazennova, E. V., Weber, J. N., Pokrovsky, V. V., Mikhailovich, V. M., and Bobkov, A. F. (2004). Diversity of human immunodeficiency virus type 1 subtype A and CRF03\_AB protease in Eastern Europe: selection of the V77I variant and its rapid spread in injecting drug user populations. *J Virol* 78(20), 11276-87.
- Rouet, F., Ekouevi, D. K., Chaix, M. L., Burgard, M., Inwoley, A., Tony, T. D., Danel, C., Anglaret, X., Leroy, V., Msellati, P., Dabis, F., and Rouzioux, C. (2005). Transfer and evaluation of an automated, low-cost real-time reverse transcription-PCR test for diagnosis and monitoring of human immunodeficiency virus type 1 infection in a West African resource-limited setting. *J Clin Microbiol* 43(6), 2709-17.
- Rouet, F., Foulongne, V., Viljoen, J., Steegen, K., Becquart, P., Valea, D., Danaviah, S., Segondy, M., Verhofstede, C., and Van de Perre, P. (2010). Comparison of the Generic HIV Viral Load assay with the Amplicor HIV-1 monitor v1.5 and Nuclisens HIV-1 EasyQ v1.2 techniques for plasma HIV-1 RNA quantitation of non-B subtypes: the Kesho Bora preparatory study. *J Virol Methods* 163(2), 253-7.
- Ryan, C. E., Elliott, J. H., Middleton, T., Mijch, A. M., Street, A. C., Hellard, M., Crofts, N., Crowe, S. M., and Oelrichs, R. B. (2004). The molecular epidemiology of HIV type 1 among Vietnamese Australian injecting drug users in Melbourne, Australia. *AIDS Res Hum Retroviruses* 20(12), 1364-7.
- Sacktor, N., Nakasujja, N., Skolasky, R. L., Rezapour, M., Robertson, K., Musisi, S., Katabira, E., Ronald, A., Clifford, D. B., Laeyendecker, O., and Quinn, T. C. (2009). HIV subtype D is associated with dementia, compared with subtype A, in immunosuppressed individuals at risk of cognitive impairment in Kampala, Uganda. *Clin Infect Dis* 49(5), 780-6.
- Santos, A. F., Abecasis, A. B., Vandamme, A. M., Camacho, R. J., and Soares, M. A. (2009). Discordant genotypic interpretation and phenotypic role of protease mutations in HIV-1 subtypes B and G. *J Antimicrob Chemother* 63(3), 593-9.
- Santos, A. F., and Soares, M. A. (2010). HIV Genetic Diversity and Drug Resistance *Viruses* 2(2), 503-531.
- Santos, A. F., Sousa, T. M., Soares, E. A., Sanabani, S., Martinez, A. M., Sprinz, E., Silveira, J., Sabino, E. C., Tanuri, A., and Soares, M. A. (2006). Characterization of a new circulating recombinant form comprising HIV-1 subtypes C and B in southern Brazil. *AIDS* 20(16), 2011-9.
- Sarrami-Forooshani, R., Das, S. R., Sabahi, F., Adeli, A., Esmaeili, R., Wahren, B., Mohraz, M., Haji-Abdolbaghi, M., Rasoolinejad, M., Jameel, S., and Mahboudi, F. (2006). Molecular analysis and phylogenetic characterization of HIV in Iran. *J Med Virol* 78(7), 853-63.

- Schable, C., Zekeng, L., Pau, C. P., Hu, D., Kaptue, L., Gurtler, L., Dondero, T., Tsague, J. M., Schochetman, G., Jaffe, H., and et al. (1994). Sensitivity of United States HIV antibody tests for detection of HIV-1 group O infections. *Lancet* 344(8933), 1333-4.
- Schuitemaker, H., van 't Wout, A. B., and Lusso, P. (2011). Clinical significance of HIV-1 coreceptor usage. *J Transl Med* 9 Suppl 1, S5.
- Scott, L. E., Noble, L. D., Moloi, J., Erasmus, L., Venter, W. D., and Stevens, W. (2009). Evaluation of the Abbott m2000 RealTime human immunodeficiency virus type 1 (HIV-1) assay for HIV load monitoring in South Africa compared to the Roche Cobas AmpliPrep-Cobas Amplicor, Roche Cobas AmpliPrep-Cobas TaqMan HIV-1, and BioMerieux NucliSENS EasyQ HIV-1 assays. *J Clin Microbiol* 47(7), 2209-17.
- Shafer, R. W. (2002). Genotypic testing for human immunodeficiency virus type 1 drug resistance. *Clin Microbiol Rev* 15(2), 247-77.
- Simon, F., Ly, T. D., Baillou-Beaufils, A., Fauveau, V., De Saint-Martin, J., Loussert-Ajaka, I., Chaix, M. L., Saragosti, S., Courouce, A. M., Ingrand, D., and et al. (1994). Sensitivity of screening kits for anti-HIV-1 subtype O antibodies. *AIDS* 8(11), 1628-9.
- Simon, F., Mauclere, P., Roques, P., Loussert-Ajaka, I., Muller-Trutwin, M. C., Saragosti, S., Georges-Courbot, M. C., Barre-Sinoussi, F., and Brun-Vezinet, F. (1998). Identification of a new human immunodeficiency virus type 1 distinct from group M and group O. *Nat Med* 4(9), 1032-7.
- Smith, R. A., Anderson, D. J., Pyrak, C. L., Preston, B. D., and Gottlieb, G. S. (2009). Antiretroviral drug resistance in HIV-2: three amino acid changes are sufficient for classwide nucleoside analogue resistance. *J Infect Dis* 199(9), 1323-6.
- Snoeck, J., Kantor, R., Shafer, R. W., Van Laethem, K., Deforche, K., Carvalho, A. P., Wynhoven, B., Soares, M. A., Cane, P., Clarke, J., Pillay, C., Sirivichayakul, S., Ariyoshi, K., Holguin, A., Rudich, H., Rodrigues, R., Bouzas, M. B., Brun-Vezinet, F., Reid, C., Cahn, P., Brigido, L. F., Grossman, Z., Soriano, V., Sugiura, W., Phanuphak, P., Morris, L., Weber, J., Pillay, D., Tanuri, A., Harrigan, R. P., Camacho, R., Schapiro, J. M., Katzenstein, D., and Vandamme, A. M. (2006). Discordances between interpretation algorithms for genotypic resistance to protease and reverse transcriptase inhibitors of human immunodeficiency virus are subtype dependent. *Antimicrob Agents Chemother* 50(2), 694-701.
- Soares, E., Makamche, M., Siqueira, J., Lumngwena, E., Mbuagbaw, J., Kaptue, L., Asonganyi, T., Seuáñez, H., Soares, M., and Alemnji, G. (2010). Molecular diversity and polymerase gene genotypes of HIV-1 among treatment-naïve Cameroonian subjects with advanced disease. *J. Clin Virol.* 48(3), 173-179.
- Songok, E. M., Lwembe, R. M., Kibaya, R., Kobayashi, K., Ndembi, N., Kita, K., Vulule, J., Oishi, I., Okoth, F., Kageyama, S., and Ichimura, H. (2004). Active generation and selection for HIV intersubtype A/D recombinant forms in a coinfecting patient in Kenya. *AIDS Res Hum Retroviruses* 20(2), 255-8.
- Soto-Ramirez, L., Renjifo, B., McLane, M., Marlink, R., O'Hara, C., Sutthent, R., Wasi, C., Vithayasai, P., Vithayasai, V., Apichartpiyakul, C., Auewarakul, P., Peña-Cruz, V., Chui, D., Osathanondh, R., Mayer, K., Lee, T., and Essex, M. (1996). HIV-1 Langerhans' cell tropism associated with heterosexual transmission of HIV. *Science* 271(5253), 1291-3.
- Spivak, A. M., Sydnor, E. R., Blankson, J. N., and Gallant, J. E. (2010). Seronegative HIV-1 infection: a review of the literature. *AIDS* 24(10), 1407-14.
- Stevens, W., Sherman, G., Downing, R., Parsons, L. M., Ou, C. Y., Crowley, S., Gershly-Damet, G. M., Fransen, K., Bulterys, M., Lu, L., Homsy, J., Finkbeiner, T., and



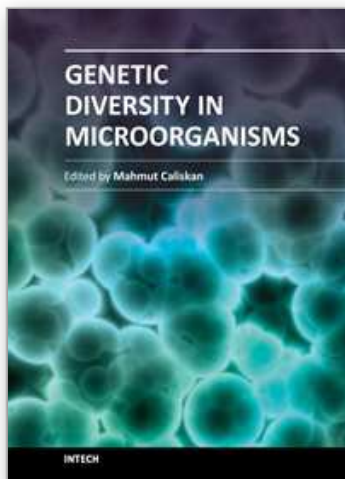
- Nkengasong, J. N. (2008). Role of the laboratory in ensuring global access to ARV treatment for HIV-infected children: consensus statement on the performance of laboratory assays for early infant diagnosis. *Open AIDS J* 2, 17-25.
- Stevens, W., Wiggill, T., Horsfield, P., Coetzee, L., and Scott, L. E. (2005). Evaluation of the NucliSens EasyQ assay in HIV-1-infected individuals in South Africa. *J Virol Methods* 124(1-2), 105-10.
- Sun, R., Ku, J., Jayakar, H., Kuo, J. C., Brambilla, D., Herman, S., Rosenstrauss, M., and Spadaro, J. (1998). Ultrasensitive reverse transcription-PCR assay for quantitation of human immunodeficiency virus type 1 RNA in plasma. *J Clin Microbiol* 36(10), 2964-9.
- Swanson, P., de Mendoza, C., Joshi, Y., Golden, A., Hodinka, R. L., Soriano, V., Devare, S. G., and Hackett, J., Jr. (2005). Impact of human immunodeficiency virus type 1 (HIV-1) genetic diversity on performance of four commercial viral load assays: LCx HIV RNA Quantitative, AMPLICOR HIV-1 MONITOR v1.5, VERSANT HIV-1 RNA 3.0, and NucliSens HIV-1 QT. *J Clin Microbiol* 43(8), 3860-8.
- Swanson, P., Holzmayer, V., Huang, S., Hay, P., Adebiyi, A., Rice, P., Abravaya, K., Thamm, S., Devare, S. G., and Hackett, J., Jr. (2006). Performance of the automated Abbott RealTime HIV-1 assay on a genetically diverse panel of specimens from London: comparison to VERSANT HIV-1 RNA 3.0, AMPLICOR HIV-1 MONITOR v1.5, and LCx HIV RNA Quantitative assays. *J Virol Methods* 137(2), 184-92.
- Swanson, P., Huang, S., Abravaya, K., de Mendoza, C., Soriano, V., Devare, S. G., and Hackett, J., Jr. (2007). Evaluation of performance across the dynamic range of the Abbott RealTime HIV-1 assay as compared to VERSANT HIV-1 RNA 3.0 and AMPLICOR HIV-1 MONITOR v1.5 using serial dilutions of 39 group M and O viruses. *J Virol Methods* 141(1), 49-57.
- Tagliamonte, M., Naderi, H. R., Tornesello, M. L., Farid, R., Buonaguro, F. M., and Buonaguro, L. (2007). HIV type 1 subtype A epidemic in injecting drug user (IDU) communities in Iran. *AIDS Res Hum Retroviruses* 23(12), 1569-74.
- Tang, N., Huang, S., Salituro, J., Mak, W. B., Cloherty, G., Johanson, J., Li, Y. H., Schneider, G., Robinson, J., Hackett, J., Jr., Swanson, P., and Abravaya, K. (2007). A RealTime HIV-1 viral load assay for automated quantitation of HIV-1 RNA in genetically diverse group M subtypes A-H, group O and group N samples. *J Virol Methods* 146(1-2), 236-45.
- Tapia, N., Franco, S., Puig-Basagoiti, F., Menendez, C., Alonso, P. L., Mshinda, H., Clotet, B., Saiz, J. C., and Martinez, M. A. (2003). Influence of human immunodeficiency virus type 1 subtype on mother-to-child transmission. *J Gen Virol* 84(Pt 3), 607-13.
- Taylor, B. S., and Hammer, S. M. (2008). The challenge of HIV-1 subtype diversity. *N Engl J Med* 359(18), 1965-6.
- Taylor, S., Jayasuriya, A., and Smit, E. (2009). Using HIV resistance tests in clinical practice. *J Antimicrob Chemother* 64(2), 218-22.
- Tee, K. K., Kamarulzaman, A., and Ng, K. P. (2006). Short communication: low prevalence of genotypic drug resistance mutations among antiretroviral-naive HIV type 1 patients in Malaysia. *AIDS Res Hum Retroviruses* 22(2), 121-4.
- Tee, K. K., Li, X. J., Nohtomi, K., Ng, K. P., Kamarulzaman, A., and Takebe, Y. (2006). Identification of a novel circulating recombinant form (CRF33\_01B) disseminating widely among various risk populations in Kuala Lumpur, Malaysia. *J Acquir Immune Defic Syndr* 43(5), 523-9.
- Thompson, M. A., Aberg, J. A., Cahn, P., Montaner, J. S., Rizzardini, G., Telenti, A., Gatell, J. M., Gunthard, H. F., Hammer, S. M., Hirsch, M. S., Jacobsen, D. M., Reiss, P.,

- Richman, D. D., Volberding, P. A., Yeni, P., and Schooley, R. T. (2010). Antiretroviral treatment of adult HIV infection: 2010 recommendations of the International AIDS Society-USA panel. *JAMA* 304(3), 321-33.
- Toni, T. D., Masquelier, B., Lazaro, E., Dore-Mbami, M., Ba-Gomis, F. O., Tea-Diop, Y., Kouakou, K., Diby, J., Sia, E., Soppi, S., Essien, S., Schrive, M. H., Pinson, P., Chenal, H., and Fleury, H. J. (2005). Characterization of nevirapine (NVP) resistance mutations and HIV type 1 subtype in women from Abidjan (Cote d'Ivoire) after NVP single-dose prophylaxis of HIV type 1 mother-to-child transmission. *AIDS Res Hum Retroviruses* 21(12), 1031-4.
- Torimiro, J. N., D'Arrigo, R., Takou, D., Nanfack, A., Pizzi, D., Ngong, I., Carr, J. K., Joseph, F. P., Perno, C. F., and Cappelli, G. (2009). Human immunodeficiency virus type 1 intersubtype recombinants predominate in the AIDS epidemic in Cameroon. *New Microbiol* 32(4), 325-31.
- Tovanabutra, S., Kijak, G. H., Beyrer, C., Gammon-Richardson, C., Sakkhachornphop, S., Vongchak, T., Jittiwutikarn, J., Razak, M. H., Sanders-Buell, E., Robb, M. L., Suriyanon, V., Birx, D. L., Michael, N. L., Celentano, D. D., and McCutchan, F. E. (2007). Identification of CRF34\_01B, a second circulating recombinant form unrelated to and more complex than CRF15\_01B, among injecting drug users in northern Thailand. *AIDS Res Hum Retroviruses* 23(6), 829-33.
- Tovanabutra, S., Watanaveeradej, V., Viputtikul, K., De Souza, M., Razak, M. H., Suriyanon, V., Jittiwutikarn, J., Sriplienchan, S., Nitayaphan, S., Benenson, M. W., Sirisopana, N., Renzullo, P. O., Brown, A. E., Robb, M. L., Beyrer, C., Celentano, D. D., McNeil, J. G., Birx, D. L., Carr, J. K., and McCutchan, F. E. (2003). A new circulating recombinant form, CRF15\_01B, reinforces the linkage between IDU and heterosexual epidemics in Thailand. *AIDS Res Hum Retroviruses* 19(7), 561-7.
- Trevino, A., Soriano, V., Rodriguez, C., Arredondo, M., Rivas, P., Herrero-Mendoza, D., Parra, P., Del Romero, J., Anta, L., Puente, S., and de Mendoza, C. (2011). Changing Rate of Non-B Subtypes and Coinfection with Hepatitis B/C Viruses in Newly Diagnosed HIV Type 1 Individuals in Spain. *AIDS Res Hum Retroviruses* 27(6), 633-638.
- Triques, K., Bourgeois, A., Saragosti, S., Vidal, N., Mpoudi-Ngole, E., Nzilambi, N., Apetrei, C., Ekwilanga, M., Delaporte, E., and Peeters, M. (1999). High diversity of HIV-1 subtype F strains in Central Africa. *Virology* 259(1), 99-109.
- Triques, K., Bourgeois, A., Vidal, N., Mpoudi-Ngole, E., Mulanga-Kabeya, C., Nzilambi, N., Torimiro, N., Saman, E., Delaporte, E., and Peeters, M. (2000). Near-full-length genome sequencing of divergent African HIV type 1 subtype F viruses leads to the identification of a new HIV type 1 subtype designated K. *AIDS Res Hum Retroviruses* 16(2), 139-51.
- Tscherning-Casper, C., Dolcini, G., Maucelere, P., Fenyo, E. M., Barre-Sinoussi, F., Albert, J., and Menu, E. (2000). Evidence of the existence of a new circulating recombinant form of HIV type 1 subtype A/J in Cameroon. The European Network on the Study of In Utero Transmission of HIV-1. *AIDS Res Hum Retroviruses* 16(13), 1313-8.
- Tscherning, C., Alaeus, A., Fredriksson, R., Bjorndal, A., Deng, H., Littman, D. R., Fenyo, E. M., and Albert, J. (1998). Differences in chemokine coreceptor usage between genetic subtypes of HIV-1. *Virology* 241(2), 181-8.
- Turner, D., Shahar, E., Katchman, E., Kedem, E., Matus, N., Katzir, M., Hassoun, G., Pollack, S., Kessner, R., Wainberg, M. A., and Avidor, B. (2009). Prevalence of the K65R resistance reverse transcriptase mutation in different HIV-1 subtypes in Israel. *J Med Virol* 81(9), 1509-12.

- Vallari, A., Bodelle, P., Ngansop, C., Makamche, F., Ndembi, N., Mbanya, D., Kaptue, L., Gurtler, L. G., McArthur, C. P., Devare, S. G., and Brennan, C. A. (2010). Four new HIV-1 group N isolates from Cameroon: Prevalence continues to be low. *AIDS Res Hum Retroviruses* 26(1), 109-15.
- Vallari, A., Holzmayr, V., Harris, B., Yamaguchi, J., Ngansop, C., Makamche, F., Mbanya, D., Kaptue, L., Ndembi, N., Gurtler, L., Devare, S., and Brennan, C. A. (2011). Confirmation of Putative HIV-1 Group P in Cameroon. *J Virol* 85, 1403-1407.
- van Binsbergen, J., de Rijk, D., Peels, H., Dries, C., Scherders, J., Koolen, M., Zekeng, L., and Gurtler, L. G. (1996). Evaluation of a new third generation anti-HIV-1/anti-HIV-2 assay with increased sensitivity for HIV-1 group O. *J Virol Methods* 60(2), 131-7.
- van Deursen, P., Oosterlaken, T., Andre, P., Verhoeven, A., Bertens, L., Trabaud, M. A., Ligeon, V., and de Jong, J. (2010). Measuring human immunodeficiency virus type 1 RNA loads in dried blood spot specimens using NucliSENS EasyQ HIV-1 v2.0. *J Clin Virol* 47(2), 120-5.
- Vandamme, A. M., Camacho, R. J., Ceccherini-Silberstein, F., De Luca, A., Palmisano, L., Paraskevis, D., Paredes, R., Poljak, M., Schmit, J. C., Soriano, V., Walter, H., and Sonnerborg, A. (2011). European Recommendations for the Clinical Use of HIV Drug Resistance Testing: 2011 Update. *AIDS Rev* 13(2), 77-108.
- Vandamme, A. M., Sonnerborg, A., Ait-Khaled, M., Albert, J., Asjo, B., Bachelier, L., Banhegyi, D., Boucher, C., Brun-Vezinet, F., Camacho, R., Clevenbergh, P., Clumeck, N., Dedes, N., De Luca, A., Doerr, H. W., Faudon, J. L., Gatti, G., Gerstoft, J., Hall, W. W., Hatzakis, A., Hellmann, N., Horban, A., Lundgren, J. D., Kempf, D., Miller, M., Miller, V., Myers, T. W., Nielsen, C., Opravil, M., Palmisano, L., Perno, C. F., Phillips, A., Pillay, D., Pumarola, T., Ruiz, L., Salminen, M., Schapiro, J., Schmidt, B., Schmit, J. C., Schuurman, R., Shulse, E., Soriano, V., Staszewski, S., Vella, S., Youle, M., Ziermann, R., and Perrin, L. (2004). Updated European recommendations for the clinical use of HIV drug resistance testing. *Antivir Ther* 9(6), 829-48.
- Vandekerckhove, L., Wensing, A., Kaiser, R., Brun-Vezinet, F., Clotet, B., De Luca, A., Dressler, S., Garcia, F., Geretti, A., Klimkait, T., Korn, K., Masquelier, B., Perno, C., Schapiro, J., Soriano, V., Sonnerborg, A., Vandamme, A. M., Verhofstede, C., Walter, H., Zazzi, M., and Boucher, C. (2011). European guidelines on the clinical management of HIV-1 tropism testing. *Lancet Infect Dis* 11(5), 394-407.
- Vazquez de Parga, E., Rakhmanova, A., Perez-Alvarez, L., Vinogradova, A., Delgado, E., Thomson, M. M., Casado, G., Sierra, M., Munoz, M., Carmona, R., Vega, Y., Contreras, G., Medrano, L., Osmanov, S., and Najera, R. (2005). Analysis of drug resistance-associated mutations in treatment-naive individuals infected with different genetic forms of HIV-1 circulating in countries of the former Soviet Union. *J Med Virol* 77(3), 337-44.
- Vergne, L., Snoeck, J., Aghokeng, A., Maes, B., Valea, D., Delaporte, E., Vandamme, A. M., Peeters, M., and Van Laethem, K. (2006a). Genotypic drug resistance interpretation algorithms display high levels of discordance when applied to non-B strains from HIV-1 naive and treated patients. *FEMS Immunol Med Microbiol* 46(1), 53-62.
- Vergne, L., Stuyver, L., Van Houtte, M., Butel, C., Delaporte, E., and Peeters, M. (2006b). Natural polymorphism in protease and reverse transcriptase genes and in vitro antiretroviral drug susceptibilities of non-B HIV-1 strains from treatment-naive patients. *J Clin Virol* 36(1), 43-9.
- Vidal, N., Bazepeo, S. E., Mulanga, C., Delaporte, E., and Peeters, M. (2009). Genetic characterization of eight full-length HIV type 1 genomes from the Democratic

- Republic of Congo (DRC) reveal a new subsubtype, A5, in the A radiation that predominates in the recombinant structure of CRF26\_A5U. *AIDS Res Hum Retroviruses* 25(8), 823-32.
- Vidal, N., Mulanga, C., Bazepeo, S. E., Lepira, F., Delaporte, E., and Peeters, M. (2006). Identification and molecular characterization of subsubtype A4 in central Africa. *AIDS Res Hum Retroviruses* 22(2), 182-7.
- Wainberg, M. A., and Brenner, B. G. (2010). Role of HIV Subtype Diversity in the Development of Resistance to Antiviral Drugs *Viruses* 2, 2493-2508.
- Waters, L., Kambugu, A., Tibenderana, H., Meya, D., John, L., Mandalia, S., Nabankema, M., Namugga, I., Quinn, T. C., Gazzard, B., Reynolds, S. J., and Nelson, M. (2007). Evaluation of filter paper transfer of whole-blood and plasma samples for quantifying HIV RNA in subjects on antiretroviral therapy in Uganda. *J Acquir Immune Defic Syndr* 46(5), 590-3.
- Weber, B. (2002). Human immunodeficiency virus (HIV) antigen-antibody combination assays: evaluation of HIV seroconversion sensitivity and subtype detection. *J Clin Microbiol* 40(11), 4402-3; author reply 4403-4.
- Weber, B., Fall, E. H., Berger, A., and Doerr, H. W. (1998). Reduction of diagnostic window by new fourth-generation human immunodeficiency virus screening assays. *J Clin Microbiol* 36(8), 2235-9.
- Wensing, A. M., van de Vijver, D. A., Angarano, G., Asjo, B., Balotta, C., Boeri, E., Camacho, R., Chaix, M. L., Costagliola, D., De Luca, A., Derdelinckx, I., Grossman, Z., Hamouda, O., Hatzakis, A., Hemmer, R., Hoepelman, A., Horban, A., Korn, K., Kucherer, C., Leitner, T., Loveday, C., MacRae, E., Maljkovic, I., de Mendoza, C., Meyer, L., Nielsen, C., Op de Coul, E. L., Ormaasen, V., Paraskevis, D., Perrin, L., Puchhammer-Stockl, E., Ruiz, L., Salminen, M., Schmit, J. C., Schneider, F., Schuurman, R., Soriano, V., Stanczak, G., Stanojevic, M., Vandamme, A. M., Van Laethem, K., Violin, M., Wilbe, K., Yerly, S., Zazzi, M., and Boucher, C. A. (2005). Prevalence of drug-resistant HIV-1 variants in untreated individuals in Europe: implications for clinical management. *J Infect Dis* 192(6), 958-66.
- Wilbe, K., Casper, C., Albert, J., and Leitner, T. (2002). Identification of two CRF11-cpx genomes and two preliminary representatives of a new circulating recombinant form (CRF13-cpx) of HIV type 1 in Cameroon. *AIDS Res Hum Retroviruses* 18(12), 849-56.
- Wirten, M., Tubiana, R., Marguet, F., Leroy, I., Simon, A., Bonmarchand, M., Ait-Arkoub, Z., Murphy, R., Marcelin, A. G., Katlama, C., and Calvez, V. (2009). Impact of discrepancies between the Abbott realtime and cobas TaqMan assays for quantification of human immunodeficiency virus type 1 group M non-B subtypes. *J Clin Microbiol* 47(5), 1543-5.
- Wolinsky, S. M., Wike, C. M., Korber, B. T., Hutto, C., Parks, W. P., Rosenblum, L. L., Kunstman, K. J., Furtado, M. R., and Munoz, J. L. (1992). Selective transmission of human immunodeficiency virus type-1 variants from mothers to infants. *Science* 255(5048), 1134-7.
- (June 2010). Technical Brief on HIV Viral Load Technologies World Health Organization.
- Wu, X., Parast, A. B., Richardson, B. A., Nduati, R., John-Stewart, G., Mbori-Ngacha, D., Rainwater, S. M., and Overbaugh, J. (2006). Neutralization escape variants of human immunodeficiency virus type 1 are transmitted from mother to infant. *J Virol* 80(2), 835-44.

- Xu, S., Song, A., Li, X., Li, J., Bao, Z., Mao, P., Zhao, Q., and Wang, Y. (2008). Performance of the Abbott RealTime HIV-1 assay for quantification of HIV-1 clades prevalent in China. *J Clin Virol* 41(4), 305-9.
- Yamaguchi, J., Badreddine, S., Swanson, P., Bodelle, P., Devare, S. G., and Brennan, C. A. (2008). Identification of new CRF43\_02G and CRF25\_cpx in Saudi Arabia based on full genome sequence analysis of six HIV type 1 isolates. *AIDS Res Hum Retroviruses* 24(10), 1327-35.
- Yamaguchi, J., Bodelle, P., Vallari, A. S., Coffey, R., McArthur, C. P., Schochetman, G., Devare, S. G., and Brennan, C. A. (2004). HIV infections in northwestern Cameroon: identification of HIV type 1 group O and dual HIV type 1 group M and group O infections. *AIDS Res Hum Retroviruses* 20(9), 944-57.
- Yamaguchi, J., Vallari, A., Ngansop, C., Makamche, F., Ndembi, N., Mbanya, D., Kaptue, L., Gurtler, L. G., Devare, S. G., and Brennan, C. A. (2010). Near full-length sequence of HIV type 1 subtype J strain 04CMU11421 from Cameroon. *AIDS Res Hum Retroviruses* 26(6), 693-7.
- Yang, C., Li, M., Newman, R. D., Shi, Y. P., Ayisi, J., van Eijk, A. M., Otieno, J., Misore, A. O., Steketee, R. W., Nahlen, B. L., and Lal, R. B. (2003). Genetic diversity of HIV-1 in western Kenya: subtype-specific differences in mother-to-child transmission. *AIDS* 17(11), 1667-74.
- Yao, J., Liu, Z., Ko, L. S., Pan, G., and Jiang, Y. (2005). Quantitative detection of HIV-1 RNA using NucliSens EasyQ HIV-1 assay. *J Virol Methods* 129(1), 40-6.
- Yebra, G., de Mulder, M., del Romero, J., Rodriguez, C., and Holguin, A. HIV-1 non-B subtypes: High transmitted NNRTI-resistance in Spain and impaired genotypic resistance interpretation due to variability. *Antiviral Res* 85(2), 409-17.
- Young, T. P., Cloherty, G., Fransen, S., Napolitano, L., Swanson, P., Herman, C., Parkin, N. T., and Hackett, J., Jr. (2011). Performance of the Abbott RealTime HIV-1 viral load assay is not impacted by integrase inhibitor resistance-associated mutations. *J Clin Microbiol* 49(4), 1631-4.
- Zhang, H., Rola, M., West, J. T., Tully, D. C., Kubis, P., He, J., Kankasa, C., and Wood, C. (2010a). Functional properties of the HIV-1 subtype C envelope glycoprotein associated with mother-to-child transmission. *Virology* 400(2), 164-74.
- Zhang, H., Tully, D. C., Hoffmann, F. G., He, J., Kankasa, C., and Wood, C. (2010b). Restricted genetic diversity of HIV-1 subtype C envelope glycoprotein from perinatally infected Zambian infants. *PLoS One* 5(2), e9294.
- Zhao, J., Tang, S., Ragupathy, V., Carr, J. K., Wolfe, N. D., Awazi, B., and Hewlett, I. (2010). Identification and genetic characterization of a novel CRF22\_01A1 recombinant form of HIV type 1 in Cameroon. *AIDS Res Hum Retroviruses* 26(9), 1033-45.
- Zolfo, M., Schapiro, J. M., Phan, V., Koole, O., Thai, S., Vekemans, M., Fransen, K., and Lynen, L. (2010 Set 22 [Epub ahead of print]). Genotypic Impact of Prolonged Detectable HIV Type 1 RNA Viral Load after HAART Failure in a CRF01\_AE-Infected Cohort. *AIDS Res Hum Retroviruses*.
- Zouhair, S., Roussin-Bretagne, S., Moreau, A., Brunet, S., Laperche, S., Maniez, M., Barin, F., and Harzic, M. (2006). Group o human immunodeficiency virus type 1 infection that escaped detection in two immunoassays. *J Clin Microbiol* 44(2), 662-5.



## **Genetic Diversity in Microorganisms**

Edited by Prof. Mahmut Caliskan

ISBN 978-953-51-0064-5

Hard cover, 382 pages

**Publisher** InTech

**Published online** 24, February, 2012

**Published in print edition** February, 2012

Genetic Diversity in Microorganisms presents chapters revealing the magnitude of genetic diversity of microorganisms living in different environmental conditions. The complexity and diversity of microbial populations is by far the highest among all living organisms. The diversity of microbial communities and their ecologic roles are being explored in soil, water, on plants and in animals, and in extreme environments such as the arctic deep-sea vents or high saline lakes. The increasing availability of PCR-based molecular markers allows the detailed analyses and evaluation of genetic diversity in microorganisms. The purpose of the book is to provide a glimpse into the dynamic process of genetic diversity of microorganisms by presenting the thoughts of scientists who are engaged in the generation of new ideas and techniques employed for the assessment of genetic diversity, often from very different perspectives. The book should prove useful to students, researchers, and experts in the area of microbial phylogeny, genetic diversity, and molecular biology.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Inês Bártolo and Nuno Taveira (2012). HIV-1 Diversity and Its Implications in Diagnosis, Transmission, Disease Progression, and Antiretroviral Therapy, Genetic Diversity in Microorganisms, Prof. Mahmut Caliskan (Ed.), ISBN: 978-953-51-0064-5, InTech, Available from: <http://www.intechopen.com/books/genetic-diversity-in-microorganisms/hiv-1-diversity-and-its-implications-in-diagnosis-transmission-disease-progression-and-antiretrovira>

**INTECH**  
open science | open minds

### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen