The application of HIV-1 proviral DNA in patients with low-level viraemia under antiretroviral therapy

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Background
One possible approach to characterize drug resistance of low-level viremia (LLV) patients is to sequence HIV proviral DNA. This study analyzed the drug resistance characteristics in DNA of HIV/AIDS patients who developed LLV after antiretroviral therapy (ART) in a hospital in Beijing and evaluated its reliability compared to RNA genotypic resistance test (GRT).

Materials and methods
Peripheral venous blood was collected from HIV-1 infected patients who had been routinely receiving ART for ≥6 months at the STD/AIDS clinic of Beijing Youan Hospital between January 2020 to September 2021 and who developed LLV. HIV-1 DNA and RNA were extracted from concentrated white blood cells and plasma respectively, and the pol gene region of HIV-1 virus was amplified. Combined with past RNA genotype, DNA and RNA genotypes were categorized into three groups: DNA genotypes compared with past RNA genotypes (group 1); comparing with RNA genotypes on the same day (group 2); comparing with past RNA genotypes and RNA genotypes on the same day (group 3).

Results
A total of 154 plasma samples with a viral load of 50-999 copies/mL were collected from 150 patients (Table 1), and 120 sequences were successfully amplified from 108 patients (77.9% amplification success rate). The resistance mutations were identified in 32 patients, with an overall resistance mutation rate of 29.6% (32/108) among which non-nucleoside reverse transcriptase inhibitors (NNRTIs)-associated resistance mutations predominated, accounting for 24.1% (26/108), followed by nucleoside reverse transcriptase inhibitors (NRTIs)-associated mutations and protease inhibitors (PIs)-associated mutations, accounting for 10.2% (11/108) and 5.6% (6/108) respectively. Of the 56, 89 and 47 patients included in groups 1, 2 and 3, the concordance rate of DNA drug resistance mutations were 73.0% (65/89), 75.0% (42/56) and 66.0% (31/47) respectively. Compared with past RNA genotypes, the loss of drug resistance mutations information in DNA genotypes can be obviously examined within all classes of ARVs (Figure 1).

Conclusions
Among LLV patients in Beijing, the drug resistance mutation rate is relatively more common with NNRTIs-related resistance predominating. In the case of LLV, DNA GRT can provide certain resistance information, but the results of RNA GRT is still the gold standard to guide the adjustment of treatment regimens.