Detection of HIV-1 Subtypes with In Vitro Diagnostic Devices

The human immunodeficiency virus 1 (HIV-1) prevalent in Germany is reflected by its subtype B. During the years 2000 to 2010, mutations HIV-subtype B have caused several false-negative HIV test results, and two HIV transmissions by blood transfusion were experienced. Consequently, the Paul-Ehrlich-Institut introduced compulsory dual-target-NAT testing for blood donations, and since then no further transmission was observed. Now, researchers of the Paul-Ehrlich-Institut and the South African national blood service jointly checked seven CE marked NAT test systems. The Journal of Clinical Virology reports on the study in its online version of 23 September 2020.

In Germany, blood donations are tested for different infectious pathogens including human immunodeficiency virus type 1 (HIV-1). Some years ago, false negative results were experienced with HIV tests performed on blood donations from HIV-1 infected persons. In Germany, this led to a transmission of HIV by donating blood in 2007 and another one in 2010. HIV-1 testing in each case was done by nucleic acid amplification tests (NAT; e.g. polymerase chain reaction, PCR). The technology is based on amplifying certain gene sections of the virus, which are then detected. At that time, naturally occurring genetic changes (mutations) in the genome of the virus were detected by researchers of the Paul-Ehrlich-Institut and other institutes as the cause of the false negative results. The mutations had occurred in the target regions of the virus genome used by the NAT test. Consequently, in 2012, the Paul-Ehrlich-Institut in its responsibility for assuring blood safety requested at least two different sections of the virus genome to be amplified independently from each other (so-called “Dual-Target-NAT”). Thus, if a mutation occurs in one target region, the second region will compensate for the potential failure and assure detection of the virus. After this measure had been introduced, no further respective incidents were observed in Germany.

In-vitro diagnostic medical devices – differences shown in HIV-1 subtype-B and HIV-1 subtype C detection

Cases of false negative results from “mono target NATs” were described in Europe and Canada, where HIV-1 subtype B prevails. However, on a world-wide basis, HIV-1 subtype B accounts for only eleven percent of the HIV infections. The most frequent subtype is HIV-1 subtype C, accounting globally for 48 percent of HIV-1 infections. Hotspots are India and South Africa, where 98 percent of the HIV-1 infections are caused by subtype C.

To study whether mutations similar to those occurring with HIV-1 subtype B, with the respective consequences for NAT testing, also occur in HIV-1 subtype C, researchers of the Paul-Ehrlich-Institut in close cooperation with the South African blood donation service studied 398 plasma samples of HIV infected blood donors from South Africa. Seven of the HIV-1 NATs available on the European market reflecting different designs (mono target, dual target; different target regions) were studied. Other than for subtype B, all HIV-1 subtype C samples were tested positive by all seven NATs, including mono-target NATs. Furthermore, there was high agreement of viral load numbers between the six quantitative NATs, independently of test design and manufacturer.

“The results confirm on the one hand that HIV-1 subtype C, globally the most frequent HIV-1 subtype, is reliably detected. In addition, the good agreement between different NATs shows that the international standardisation efforts...
for these important in vitro diagnostic devices have been successful", as PD Dr Micha Nübling, Head of Division Major Policy Issues, Co-ordination, of the Paul-Ehrlich-Institut, explains the meaning of the results.

Paul-Ehrlich-Institut – Collaboration Centre of the World Health Organisation WHO

As a WHO Collaborating Centre for Quality Assurance of Blood Products and in vitro Diagnostic Devices, the Paul-Ehrlich-Institut is committed to the quality assurance of blood products and in vitro diagnostic medical devices world-wide. The tasks of this collaborating centre also include organising and conducting laboratory studies for the standardisation of in vitro diagnostic medical devices and the support in developing guidelines and recommendations in the field of blood safety. Furthermore, the WHO collaboration centre provides its support in international workshops and conferences addressing quality features of blood products and in-vitro diagnostic medical devices (IVD).

Originalpublikation:
DOI: 10.1016/j.jcv.2020.104649