AIDS Rev 2002;4:112-113

Hot News

Welcome to «Hot News», a section of AIDS Reviews written by the editors and invited experts which focuses on recently reported information believed to be of both impact and higher interest to the readerships.

HIV's adaptation to the human immune system

Several reports have recently illustrated HIV's surprising capabilities of adaptation to the human immune system. The group of George Pavlakis has just identified natural killer cells (NK cells) as a new hideout for HIV (Valentin, et al. Proc Natl Acad Sci USA 2002;99:7015-20), in addition to latently infected T-cells. HIV-1 DNA remains in NK cells, even after two years of aggressive treatment with combinations of three antiretroviral drugs and virus could be cultured from purified NK cells. Infection of NK cells may contribute to defects in innate immunity previously reported in AIDS patients. Strategies aimed at targeting latently infected T-cells may not affect the virus hiding in NK cells.

Another baffling achievement of the virus is its preferential infection of HIV-specific T-cells. Douek, et al. (Nature 2002;417:95-8) noticed that proviral DNA load is significantly higher in, and rebound after treatment interruption is stronger for, HIV-specific T-cells than for T-cells with any other specificity. Any vaccination strategy aimed at increasing the pool of HIV-specific T-cells may, therefore, increase the susceptibility of T-cells to infection, rather than protect those cells. Similarly, structured treatment interruption cycles may increase the proportion of HIV-specific T-cells, without improving the patient's health outcome.

A third paper provides evidence that the adaptive evolution of HIV has lead to HLA-restricted immune responses at the human population level (Moore, et al. Science 2002;296:1439-43). HIV-directed cytotoxic T lymphocytes exert a strong selective pressure on the virus. The authors identified areas of variability in the *pol* gene that were HLA class I dependent, while some areas within this region were less variable in patients with particular HLA types. This study supports the idea that HIV can escape from CTL responses and, in doing so, a viral population has been selected that is better adapted to beat our immune system in its attempts to control the virus.

Together these papers illustrate how a relatively recent human virus has, in a time period of less than a century, learned to adapt to the human immune system, resulting in poor control of HIV infection by the human host.

Anne-Mieke Vandamme
Rega Institute and University Hospitals
Katholieke Universiteit Leuven
Leuven, Belgium

Nevirapine versus Efavirenz

Non-nucleoside inhibitors of the HIV reverse transcriptase are now preferred to protease inhibitors (PI) for the treatment of HIV infection. Two main considerations account for this preference. The first is related to the low number of pills and frequency of doses when treatment with either nevirapine (NVP) or efavirenz (EFZ) is chosen. The second is related to the concern on a greater risk of lipodystrophy and lipid abnormalities taking PI, which could prone to cardiovascular events in the near future.

Although concern on a lower potency of NVP in respect to EFZ has been noticed by some authors, no studies so far have confronted face to face the efficacy and safety of these two drugs. Now, a trial (*Núñez, et al. HIV Clin Trials 2002;3:186-94*) has presented for the first time data in which NVP and EFZ were randomly prescribed to a group of drug-naive individuals in a backbone of stavudine and didanosine. In the intent-to-treat analysis at 48 weeks, 74% of patients in the EFZ group and 64% of those in the NVP had undetectable viral load (<50 copies/ml). Adverse events led to discontinuation of non-nucleosides in 13% and 8% of patients in the EFZ and NVP arms, respectively. Overall, there were no statistically significant differences between groups regarding any primary end-point. Therefore, the authors concluded that EFZ and NVP along with two nucleoside analogs may be equivalent.

Although NVP and EFZ may provide similar antiviral potency, another recent publication (*Negredo, et al. AIDS 2002;16:1383-9*) has highlighted the benefit of using NVP in patients who

have developed lipodystrophy and lipid abnormalities under PI-containing regimens. This benefit seems to be unique for NVP and has not been proven yet replacing PI by EFZ in other simplification studies. A reduction in total cholesterol and LDL-cholesterol together with an increase in HDL-cholesterol was observed after 24 weeks of replacing PI by NVP. Moreover, the number and lipid content of LDL particles was significantly reduced. All these changes are expected to reduce the risk of cardiovascular events in HIV-infected patients on antiretroviral therapy.

Juan González-Lahoz
Instituto de Salud Carlos III
Madrid, Spain

When will the next type of HIV arise?

The laboratory of Martine Peeters and Eric Delaporte in Montpellier, France, has a reputation for being at the leading edge of research aimed at understanding where HIV comes from. In a recent paper (Peeters, et al. Emerg Infect Dis 2002;451-7), they again report groundbreaking news on the prevalence of SIV in the wild. Their group took 788 monkey-meat samples at the markets of Cameroon, and tested them serologically, using a sensitive INNO-LIA test, and/or by PCR. More than one-fifth of the samples tested positive for SIV, with 13 of the 16 species tested being infected. Amplification and sequencing identified 4 new types of SIV, further increasing the genetic variability of documented SIV. This means that bush-meat handlers are continuously challenged with a plethora of SIV. The risk for zoonosis today is much higher than half a century ago, since bush-meat is a growing trade. Therefore, the question is not whether a new type of HIV will arise, but rather when it will arise, and how pathogenic it will be.

Anne-Mieke Vandamme
Rega Institute and University Hospitals
Katholieke Universiteit Leuven
Leuven, Belgium