Hot News

Similar Immunological Profiles Between Nonprogressing HIV Infection in Children and Nonpathogenic SIV Infection

In the absence of antirretroviral therapy (ART), HIV infection leads to progression to AIDS in most infected individuals. However, there is a small group of HIV-infected patients capable of spontaneously controlling HIV infection, known as the elite controllers (less than 1% of total infected population). These patients maintain undetectable levels of HIV replication, in part, due to a continuously effective HIV specific T cell response. Moreover, in HIV-infected patients with suppressed viremia under ART, a chronic activation of the immune system persist, which can be related to a poor clinical outcome including death, development of co-morbidities, AIDS and non-AIDS defining events. Indeed, several studies highlight that a high level of immune activation rather than HIV replication is the major contributing factor to progression during HIV infection.

Interestingly, non-human primates naturally infected with simian immunodeficiency virus (SIV) do not develop disease and levels of immune activation remain low, despite high levels of viral replication. Therefore, natural SIV infection deserves a deeper insight and might represent an opportunity to develop models for not only the development of an HIV vaccine but also to understand the evolution of HIV disease even in individuals with undetectable viremia.

In a recent study designed to understand and identify factors preventing HIV disease in the pediatric population (Muenchhoff et al., Sci Transl Med. 2016;8:358ra125), different immunological features were analysed among 170 nonprogressing HIV infected children maintaining CD4 T cell counts despite high levels of viremia. The authors found two key immunological patterns shared with non-pathogenic SIV infection on long-lived central memory CD4 T cells: low immune activation levels with high viral load and low CCR5 expression (main receptor of HIV to enter target cells). These findings suggest a closer similarity with the non-pathogenic features observed in natural SIV hosts than those seen in HIV-infected adults.

Although more studies are needed to determine the cellular and molecular mechanisms underlying low immune activation and nonprogression in the HIV pediatric population, these observations allow to move forward in the knowledge of the pathogenesis of HIV infection and therefore, in the development of new therapeutics strategies to prevent HIV disease and also bringing us closer to a functional HIV cure.

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Mortality in Hepatitis C Populations: Another Battle Against Drugs and Alcohol

In the era of efficacious and well-tolerated treatment for chronic hepatitis C virus (HCV) infection, there is an expanding population of individuals who achieve viral eradication. This in turn has generated a need to determine the impact of liver-related morbidity and mortality, particularly liver decompensation and hepatocellular carcinoma, in populations achieving sustained viral response (SVR), and how they correlate with that of the general population.

A recent retrospective cohort study (Innes, et al. J Hepatol. 2017;66:19-27) sought to assess these findings in a group of over 1,800 patients with SVR and different stages of liver disease, with a follow-up period of over five years after viral eradication. Patients who had achieved SVR had almost double the mortality rate than that of the general population. This association persisted when analyzing only non-cirrhotic individuals with SVR, though to a lesser degree. Illegal drug-related deaths and hepatocellular carcinoma were the two main contributors towards the excess mortality seen in the study population, illegal drug use accounting for 53% of excess deaths in < 50-year-old patients, and hepatocellular carcinoma for 54% in the over 50s. The study also assessed the influence of modifiable risk factors, including intravenous drug use and alcohol abuse. It showed that a higher number of behavioral risk factors was strongly associated with higher mortality rates, whereas individuals not engaged in such behaviors showed a similar mortality to that of the general population.

Since direct-acting antivirals against HCV currently provide high cure rates with a very favorable adverse event profile using three months therapy (Banerjee, et al. Aliment Pharmacol Ther. 2016;43:674-96), the impact of modifiable health risk behaviors on the effects of such treatments and patient life expectancy remains a cause of concern. This study highlights a need to address the management of modifiable health

risk behaviors as part of chronic HCV treatment. Similar to HIV prevention strategies, pharmacological interventions alone are not sufficient to maximize the potential of antiviral therapies (Kojima, et al. AIDS. 2016;30:2251-2; Midgard, et al. J Hepatol. 2016; 65[Suppl]:33-45). Due to local variability in services, there is currently no standardized approach to incorporating risk behavior reduction into chronic HCV management. Further research should aim to ascertain the optimum method of achieving and maintaining risk behavior reductions, as well as assessing whether risk modification prior to initiating treatment provides significantly better long-term outcomes. Arguably, not addressing the motivations driving HCV infection in intravenous drug users limits the efficacy of antiviral therapy. Thus, behavioral interventions are crucial for making a significant impact in HCV patients' life expectancy.

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Transmission of Multi-Drug Resistant HIV-1 Despite Antiretroviral Prophylaxis

In Brazil, a nurse recently became infected with HIV-1 despite beginning antiretroviral therapy within one hour following accidental needle stick injury while puncturing the forearm of an HIV-infected patient with detectable plasma viremia. Thereafter, the patient's virus was found to harbor multiple drug resistance mutations (Lopez-Lopes, et al. AIDS. 2015;29:1580-3).

A daily pill of Truvada® (tenofovir + emtricitabine) has demonstrated to reduce the risk of acquiring HIV-1 in men who have sex with men engaged in high-risk sexual practices (Grant, et al. Lancet Infect Dis. 2014;14:820-9). However, there is no complete protection. In Toronto, a 43-year-old homosexual man experienced HIV-1 seroconversion after being on pre-exposure prophylaxis (PrEP) with daily Truvada® since nearly two years before. He admitted anal sex with multiple partners during the prior 2-6 weeks. At the time of primary HIV-1 infection, plasma tenofovir concentrations were adequate, confirming that he was adherent and taken well daily Truvada®. However, the virus isolated from his blood harbored multiple drug resistance mutations at the RT (41L, 67G, 69D, 181C, 184V and 215E), protease (10I) and integrase (51Y and 92Q) genes (Knox, et al. N Engl J Med. 2017;376:501-2).

Concern on the circulation of multidrug-resistant HIV-1 has been on the rise following the report of rapid progression to AIDS in a gay male in New York who acquired a multidrug-resistant HIV-1 strain a few years ago (Markowitz, et al. Lancet. 2005;365:1031-8).

The authors concluded that PrEP alone, even in persons very adherent to Truvada®, does not ensure full protection from HIV-1 transmission, and therefore further interventions including more adequate information and efforts to reduce risky behaviors are warranted in persons engage in high-risk sexual behaviors. In this way, the spread will be halted for other sexually transmitted infections, e.g. syphilis, gonorrhea, and hepatitis C, for which there is no antimicrobial prophylaxis nor vaccine. Other experts are reasoning in a similar way, highlighting that PrEP should be part of a combination approach (and not the only tool) for HIV prevention.

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