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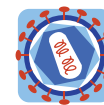
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INVITED SPEAKER PRESENTATION

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Accelerated immune senescence in HIV infection

Victor Appay

From 16th International Symposium on HIV and Emerging Infectious Diseases
Marseille, France. 24-26 March 2010

Aim

The prospect that immune activation or inflammation may be directly related to the increased incidence in HIV infected donors of manifestations that are reminiscent of the human aging process (i.e. cardiovascular disease, malignancies, osteoporosis, cognitive impairment, depression and frailty) is raising increasing concerns. On the immunological side, in addition to promoting viral replication as well as CD4⁺ T cell apoptosis, HIV associated immune activation may also lead to an accelerated decline of immune competence resembling the phenomenon of immunosenescence. Our aim is to explore further the potential relationship between immune activation, HIV disease progression and immunosenescence.

Materials and methods

We performed a comparative analysis of immunologic markers in different groups of HIV infected donors and healthy controls. The initial investigation of blood lymphocyte populations led us rapidly to turn our attention onto the lymphocyte primary immune resources, i.e. the CD34⁺ hematopoietic progenitor cells (studied directly from the blood of patients).

Results

Human aging and HIV-1 infection exhibit a number of parallels with regards to immunological attributes, that are evocative of premature immunosenescence in HIV-1 infected patients and reflect a reduced production of lymphocytes. Analyses of CD34⁺ hematopoietic progenitor cell number, phenotype and clonogenic potential underline a manifest impairment of primary immune resources with age or HIV-1 infection. Systemic immune activation emerges as a major correlate of altered lymphopoiesis, which can be partially reversed with prolonged antiretroviral therapy. Poor CD4⁺ T cell count

recovery despite successful virological response on anti-retroviral treatment is associated with persistent damage to the lymphopoietic system.

Discussion

Our findings provide new insights into the consequences of persistent immune activation in HIV-1 infection, and demonstrate the importance of primary hematopoietic resources in HIV pathogenesis and the response to antiretroviral treatments, but also more generally in the development of immunosenescence.

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