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Oral presentation

Tissue viral dynamics in SIV infected macaques with highly active antiretroviral therapy (HAART)

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Background

Under highly active antiretroviral therapy (HAART), the persistence of HIV in tissue reservoirs represent a major obstacle to viral eradication. Thus our objectives were: (1) To evaluate the viral replication and dissemination simultaneously in blood, secondary lymphoid tissues and the gut during SIV acute infection of macaque as a model of HIV infection and AIDS. (2) To assess the effect of a short term HAART initiated at different stages during SIV infection on viral dissemination and replication. (3) To correlate viral replication in tissues with local concentration of antiviral drugs.

Materials and methods

Three viral markers of viral replication and dissemination were measured in cynomolgus macaques inoculated with 50 AID: viral mRNA (viral replication), 2LTR circles (new infection), and viral DNA (viral dissemination). Blood, spleen, peripheral (inguinal and axillary) and mesenteric lymph nodes, rectum, colon and ileum were studied simultaneously in groups of 4 to 5 macaques treated with a placebo or the combination of AZT/3TC and indinavir during 14-28 days and initiated at days 0 (4 h post infection (pi)), 7, 14 and 101 pi.

Results

During acute infection, the three markers varied similarly within a same tissue. However viral replication and dissemination differ between tissues, particularly after peak of viremia. Plasma viral load decrease mainly reflects a severe decline in gut associated lymphoid tissue (GALT) viral replication whereas levels of viral mRNA and DNA remained stable in spleen and peripheral lymph nodes. Initiation of HAART before peak of viremia significantly impact on viral dissemination and replication in all tissues but did not prevent infection, even when treatment was initiated 4 h pi. Initiation of HAART, just after the viremia peak or during chronic infection, had a strong effect on virus production in plasma and GALT, but high levels of viral mRNA and DNA persist in peripheral lymph nodes and spleen. Viral replication in tissues was inversely correlated with local antiviral drugs concentrations.

Conclusion

We demonstrated the persistence of viral replication and dissemination in lymphoid tissues during primary infection. Control of viral replication in tissues is highly dependent on antiretrovirals tissular distribution.