Erythrocyte-associated HIV in a model of HIV infection

L. Fazzi[1], G. Ojeda[2], D. Gutson[3], M.M. Ávila[1], P. Pury[2], R.D. Rabinovich[1]
[1]Buenos Aires University. CONICET, Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, Buenos Aires, Argentina, [2]National University of Córdoba, School of Mathematics and Phisics, Cordoba, Argentina, [3]National University of Rio Cuarto, Departament of Computing Sciences, Rio Cuarto, Argentina

Background: Recently, binding of HIV to erythrocyte membrane has been demonstrated in infected patients, including those efficiently treated with HAART. During physiological clearance of immune complexes, erythrocytes are in close contact with spleen and liver macrophages. HIV can take advantage of this process and infect macrophages, which may act as viral reservoirs. Commonly used mathematical models for HIV replication do not consider the erythrocyte-associated HIV fraction. This study was aim to measure different parameters in this fraction and include them in such models. This can be useful for patients with undetectable viral load undergoing simplified maintenance therapies and those included in attempting viral eradication protocols.

Methods: To analyze the kinetics of attachment/ detachment of HIV to erythrocytes, the erythrocytes of 6 healthy donors were incubated with HxB2 virus at different times. After incubation, p24Ag was measured, and the amount of bound virus was calculated by the difference between the incubated virus and that measured in the erythrocyte supernatant. Extensions of Perelson's mathematical models were performed in order to include the erythrocyte-associated HIV subpopulation and two kinds of susceptible cells, T cells and macrophages.

Results: Attachment/detachment studies showed that the greater proportion of virus binding occurs in the first 5 minutes and most of it stays attached for hours on the erythrocyte membrane. Infectivity of erythrocyte-associated HIV fraction is well conserved, better than in plasma (data not shown).
The model predicts 1) the association with erythrocytes favors virus macrophagotropic variants in detriment of lymphotropic ones. 2) taking into account the assumption that viruses that emerge from macrophages in spleen and liver can bind preferentially to erythrocytes, viral replication on macrophages will be detected on erythrocytes earlier than in plasma (studies in our laboratory have shown that in patients on HAART blips are associated with virus on erythrocytes).

Conclusion: When the erythrocyte-associated HIV fraction is included in mathematical models of HIV infection, the results vary and the predictions agree with observations in patients, such as detection of virus on erythrocytes even during effective HAART. Therefore, this fraction should be considered when the kinetics of virus replication is studied.