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## Mother-to-child transmission of HTLV-I: *in vitro* study of HTLV-I passage across a tight human epithelial barrier

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Human T-Cell Leukemia Virus type 1 (HTLV-1), that infects around 15 million people world wide, is the causative agent of adult T-cell leukemia/lymphoma and HTLV-1 Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP). Besides horizontal transmission, HTLV-1 is transmitted vertically mainly through breastfeeding. This maternal transmission via breast milk appears to be the dominant mode of HTLV-1 spread in the high endemic areas, and is correlated with the presence of HTLV-1 infected cells (lymphocytes, epithelial cells...) in the milk of infected mothers.

We developed an *in vitro* model of epithelial barrier (Caco-2 human enterocytic cell line) to assess the mode of passage of HTLV-1 through the digestive tract. Integrity of the epithelial barrier was checked by ultrastructural approach (immunofluorescence for tight junction proteins, electron microscopy), measurement of the trans-epithelial resistance (TER), and diffusion of fluorescently labeled molecules (fluorescent dextran) through Transwell devices.

When the enterocytic cell line was co-cultured with HTLV-1-infected lymphocytes, no structural modifications could be detected in the tight junctions between enterocytes. Moreover, the functional integrity of the epithelial barrier was maintained since no change in TER was detected in the presence of infected lymphocytes. Similarly, the passage of small molecules (4 kDa fluorescent dextran) was

unaffected. No increase in the passage of HTLV-1 infected lymphocytes (vs uninfected) across the epithelial barrier was observed.

Although enterocytes were not found to be susceptible to HTLV-1 infection, free infectious HTLV-1 virions were detected in the basolateral compartment, and such a passage was shown to be temperature-dependent. These results suggest a transcytotic passage of virions across the enterocytes.

Our present data indicate that HTLV-1 may cross the tight epithelial barrier without disruption or alteration of its integrity, in the absence of enterocyte infection. The role of dendritic cells in HTLV-1 passage through the epithelial barrier is currently under investigation in our *in vitro* model, to further delineate the mechanisms of HTLV-1 transmission during breastfeeding.