CELLULAR PROTEINS OF THE VESICULAR TRAFFICKING PATHWAY REGULATE HTLV-1 RETENTION IN VIRAL BIOFILM AND INFECTIVITY OF CHRONICALLY INFECTED CELLS.

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Background:
The human retrovirus HTLV-1 is transmitted very efficiently after cell-cell contacts between the infected virus-producing cells and the target cells. While this mechanism is essential for HTLV-1 infection cycle, it remains a poorly. Among the three cell-cell processes of viral transmission described so far, transfer of viral biofilms accounts for 80% of productive infections measured *in vitro*. Viral biofilm encompasses neosynthesized virions trapped in adhesive extracellular aggregates. Accumulation of biofilm at the surface of infected cells may favor adherence to the target cell during cell-cell contact, allowing rapid transfer of the virus, even during fleeting contact. In this study we investigated which cellular mechanisms govern biofilm production and how they could participate in the ability of viral biofilm to infect target cells.

Methods:
We analyzed published transcriptomic data and performed mass spectrometry on isolated biofilms to identify cellular candidates enriched in HTLV-1 biofilms. Candidates' localizations in the biofilm were then analyzed by confocal microscopy. Their role in biofilm assembly and/or stability and viral transmission was evaluated using shRNA silencing in chronically infected cells.

Results:
Two cellular proteins, SNAP 25 and Caveolin, both upregulated upon HTLV-1 infection, were detected in isolated biofilms. They are known to control the fusion of cellular vesicles with the plasma membrane and to regulate cellular plasma membrane tension through endocytosis, respectively. Proteomic identification was confirmed by imaging showing their close proximity to viral biofilms. Their silencing in chronically infected cell lines affected viral production and induced virions accumulation and polarization at the surface of infected cells. Accordingly, viral transmission was also impacted by the silencing of Caveolin or SNAP 25.

Conclusion:
These results suggest that vesicular trafficking is important for virions retention and/or polarization of the biofilm, and for the infectivity of chronically infected cell lines.

This study is funded by the National Institute for Medical Scientific Research (INSERM, FR), the Ecole Normale Supérieure de Lyon (ENS de Lyon, FR) and the National AIDS and Hepatitis Research Agency (ANRS, FR).