

NOVEL INSIGHTS INTO MECHANISMS OF HIV CELL-TO-CELL TRANSFER: ROLE OF "POLY-SYNAPSES"

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HIV-1 spread in lymphocytes occurs either by free viral particles, released by infected cells, or much more efficiently by direct cell-to-cell transfer through mechanisms that are still not fully elucidated. We are studying viral cell-to-cell propagation, by confocal and electron microscopy, flow-cytometry, and real-time imaging of fluorescent HIV. Liaisons between one infected and one target T cell, leading to formation of typical virological synapses, with polarized viral budding at the interface occurred in about 25% of the contacting cells. Other modes of transfer were also frequently detected. In 10% of clusters, viral particles localized along thin filopodia-like or pseudopodia-like membrane extensions, allowing transfer through remote contacts.

In 25% of the conjugates, one infected cell contacted simultaneously several targets and transmitted virus through multiple zones of Gag accumulation, that we termed "polysynapses". Polysynapses share similarities, but are distinct from classical virological synapses. In HIV-infected individuals, these structures, by promoting concomitant infection of multiple targets in the vicinity of infected cells, may facilitate exponential viral growth as well as viral escape from immune responses.

Real-time imaging of viral transfer demonstrated that these diverse situations occur simultaneously in infected cultures. The role of selected cellular and viral proteins during HIV cell-to-cell transfer is currently being explored.