Mechanisms of HIV-1 transfer from T lymphocytes to macrophages

---

A research priority for HIV-1 eradication is the elucidation of the mechanisms involved in virus dissemination, as well as the establishment and persistence of virus reservoirs. Infected myeloid cells, including macrophages (MFs) have been evidenced in most tissues of infected patients, most often as multinucleated giant cells (MGCs), and are suspected to participate in the formation of virus reservoirs, emerging as essential target cells involved in HIV-1 pathogenesis. While HIV-1 infection of myeloid cells with cell-free viral particles has been extensively analyzed, there is still a paucity in knowledge of the mechanisms that control their infection by cell-to-cell transfer. Importantly, virus dissemination by virus cell-to-cell transfer is much more efficient than the cell-free viral infection and is susceptible to escape immune system and antiretroviral therapies. Thus, it now appears essential to better characterize the mechanisms that govern the intercellular transmission from infected T lymphocytes to MFs and the implication of this transmission route in the pathogenicity. Our aim is to investigate, both at the structural and molecular levels, the mechanisms involved in cell-to-cell transfer of HIV-1 for efficient infection of MFs. In particular, we focus on the study of integrins, F-actin cytoskeleton and associated proteins in MFs. To further analyze the first intercellular contact and the two-step cell fusion process, we are developing an original microfluidic-based cell-pairing system allowing the synchronization of thousands of T-cell-myeloid cell pairs at the same z position with high and controlled fusion process.
This ambitious project will give access to crucial information for the role of myeloid cells in pathogenesis, including HIV-1 transmission, spreading and establishment of viral tissue reservoirs. Moreover, this project can open ways for the rationale development of focused new antiviral strategies.

Keywords : macrophages, HIV-1, cell-to-cell tranfer, F-actin
Authors :
References : , , ,

Authors

Verollet Christel 1, Mascarau Remy 2, Raynaud Brigitte 2, Maridonneau-Parini Isabelle 2,

1. TBIB, IPBS, Toulouse, FRANCE
2. TBIB, IPBS/CNRS/UPS, Toulouse, FRANCE