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Postdoctoral position

One position for a two-years postdoc fellowship is opened in the context of the Team "Immune Cell Signaling and Retroviral Infection" headed by Dr Serge BENICHOU at the Cochin Institute in Paris, France. The postdoc scientist will be involved in the development of an original research project focused on "**Characterization of cellular and virological factors modulating HIV-1 cell-to-cell spreading in macrophage and dentritic cell targets**".

Macrophages and dendritic cells (DCs) are HIV-1 cellular targets and participate in virus transmission, dissemination and establishment of virus reservoirs in host tissues of infected patients. While DCs and macrophages are poorly infected *in vitro* by cell-free viruses, because of the high expression of host cell restriction factors such as SAMHD1, we have revealed a very efficient SAMHD1-independent mechanism for HIV-1 cell-to-cell transfer from infected T cells and dissemination in macrophages and DCs by a two-step cell-fusion process leading to the formation of highly virus-productive multinucleated giant cells (MGCs). In the first step, infected T cells establish contacts with macrophages or DCs, resulting in the fusion with these target myeloid cells. The newly formed HIV-1 fused cells then acquire the ability to fuse with surrounding non-infected macrophages or DCs, leading to the formation of infected MGCs containing at least one T-cell nucleus coming from the initial fusion of infected T cells. This mechanism of viral cell-to-cell transfer and dissemination in myeloid cells through cell-fusion may allow for productive infection of macrophages and DCs *in vivo*, as observed in lymphoid tissues and central nervous system of infected patients. We hypothesize that this cell-fusion mode of virus cell-to-cell transmission is modulated by host cell (restriction and other factors) and viral factors (i.e., viral auxiliary proteins). After the initial fusion between infected T cells and myeloid cells, the presence and maintenance, in a new cellular environment, of at least one transcriptionally-active T cell nucleus in HIV-1-infected MGCs should result in a new transcriptional program leading to expression of cellular factors allowing phenotypical changes for long survival and high production of infectious viruses. We can also speculate that the transfer and maintenance of the T cell nucleus, already containing integrated proviral DNA, may bypass the early steps of the virus life cycle restricted by SAMHD1, APOBEC3, SERINC proteins and other non-identified cellular factors, leading to high viral expression by MGCs.

Because of the roles of macrophages and DCs for HIV-1 pathogenesis, it is essential to decipher the mechanisms that govern, control and modulate this cell-to-cell fusion mechanism for virus transfer and dissemination in these myeloid cells. Thus, the general goal of the project is to characterize host cell and viral factors, as well as cellular pathways, modulating efficient HIV-1 cell-to-cell transmission and dissemination from infected T cells to myeloid target cells. The project is focused on 3 specific objectives:

1) Analysis of the fate and maintenance of the T cell nucleus after fusion of HIV-1 infected T cells with myeloid cell targets and formation of productively infected MGCs.

2) Analysis of the role of host cell restriction factors counteracted by HIV-1 auxiliary proteins for efficient virus cell-to-cell infection of myeloid cells.

3) Identification by RNA sequencing of new host cell factors modulating HIV-1 cell-to-cell spreading in myeloid cells.

Candidates must send their applications as well as names and letters of potential referees to Dr. Serge Benichou:serge.benichou@inserm.fr.