Master Biologie Moléculaire et Cellulaire 'BMC',
Université Paris Cité - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
https://master2bdc.ijm.fr/
Fiche de Projet de Stage de M2, 2024-2025

Unité INSERM ou CNRS ou Université : Inserm U1016, CNRS UMR8104, UPC **Intitulé Equipe : Cellules immunes et infection rétrovirale** **ED d'appartenance : BioSPC** **Responsable de l'Equipe : Serge Benichou**	**Responsable du Stage : Serge Benichou** **Contacts** Adresse : Institut Cochin, 22 rue Méchain, 75014 Paris Email : serge.benichou@inserm.fr Tel : 0609568283

Titre du projet: Characterization of the cell-cell fusion process for HIV-1 spreading in macrophages

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

Infected **macrophages** have been evidenced in many tissues of HIV-1-infected patients , very often as **multinucleated giant cells (MGCs)**, and participate in the different steps of the pathogenesis, including virus transmission, dissemination, and establishment of virus reservoirs. At least *in vitro*, macrophages are difficult to infect by cell-free virus particles. This block in virus replication is partly related to the high expression of host cell restriction factors that inhibit post-entry steps of the viral life cycle. In addition to cell-free virus infection, it is now established that HIV-1 also infect target cells through cell-to-cell transfer involving direct contacts between infected cells and uninfected target cells. We have revealed that HIV-1 uses a cell-cell fusion mechanism for virus transfer and dissemination from infected CD4+ T cells to macrophages leading to the formation of highly virus-productive MGCs (Bracq, 2017; Raynaud, 2018; Xie, 2019; Han, 2022; Mascarau, 2023), reminiscent of the macrophage-derived multinucleated cells found in tissues of infected patients.
Therefore, **the general goal of our project is to characterize the mechanisms that govern, control and modulate this cell-cell fusion process for virus transfer and dissemination from infected T cells to macrophages**. This project is focused on 2 specific objectives:

1) Candidate approach for identification of cellular factors modulating HIV-1-mediated cell-cell fusion for cell-to-cell infection of macrophages. The goal is to analyze the specific contribution of the candidate factors identified from an RNA sequencing transcriptomic analysis to the cell-cell fusion of infected T cells for virus transfer in myeloid cells.

2) Genetic screening for characterization of cellular factors modulating HIV-1-mediated cell-cell fusion for cell-to-cell infection of macrophages. The goal is to perform a large-scale screening for identification of cellular factors modulating HIV-1-mediated cell-cell fusion, first using a custom-designed arrayed sgRNA library targeting 300 genes coding for transmembrane proteins.

Publications de l'équipe relatives au projet de stage (max 5)

Mascarau, R., Woottum, M., et al. (2023) Productive HIV-1 infection of tissue macrophages by fusion with infected CD4+ T cells. J. Cell Biol., 222(5): e202205103.

Han, M., Cantaloube-Ferrieu, V., Xie, M., Armani-Tourret, M., Woottum, M., Pagès, J.-C., Colin, P., Lagane, B. and Benichou, S. (2022) HIV-1 cell-to-cell spread overcomes the virus entry block of non-macrophage-tropic strains in macrophages. PLoS Pathogens, 18(5): e1010335.

Han, M., Woottum, M., Mascarau, R., Vahlas, Z., Verollet, C. and Benichou, S. (2022) Mechanisms of HIV-1 cell-to-cell transfer in myeloid cells. J. Leuk. Biol., 1-11.

Xie, M., Leroy, H., et al. (2019) Cell-to-cell fusion for HIV1 spreading and SAMHD1-independent productive infection of myeloid target cells. mBio 10(6), e02457-19.

Bracq, L., Xie, M., Lambelé, M., Matz, J., Schmitt, A., Bouchet, J., and Benichou, S. (2017). T cell-macrophage fusion triggers multinucleated giant cell formation for HIV-1 spreading. J. Virol., 91, e01237-17