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, 2025-2026

Unité INSERM ou CNRS ou Université : **Inserm U1334, CNRS UMR8175, Université Paris Cité** **Intitulé Equipe : Transport Extracellulaire** **ED d'appartenance : BioSPC** **Responsable de l'Equipe : Grégory Lavieu**	**Responsable du Stage : Serge Benichou** **Contacts** Adresse : 22 rue Méchain, 75014 Paris Email : serge.benichou@inserm.fr Tel : 0609568283

Titre du projet : Exploring HIV-1 cell-to-cell infection of macrophages: a comprehensive in vivo and in vitro study

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

Substantial evidence indicates that **cell-to-cell transfer of HIV-1** by direct contact between infected virus-donor cells and recipient target cells represents the dominant mode of virus dissemination in vivo. At least in vitro, this mode of virus transfer is highly efficient for spreading the virus to target cells, such as **macrophages**, that are poorly susceptible to cell-free virus infection but were detected in vivo in many tissues. Remarkably, these infected myeloid cells were frequently found as **multinucleated giant cells (MGCs) in tissues**. Cell-to-cell virus dissemination may allow the virus to evade immune system clearance and antiretroviral drugs. While cell-to-cell infection of CD4 T cells through the formation of the virological synapse or other cell-to-cell mechanisms have been extensively described in vitro, recent reports demonstrate that **myeloid cells can also be productively infected through cell-to-cell virus transfer**, leading to more efficient viral spread in these otherwise poorly susceptible cells.
At least in vitro, this cell-to-cell route of HIV-1 macrophage infection primarily involves **homotypic cell-cell fusion between macrophages, or heterotypic fusion between infected T cells and macrophages**. Both processes lead to the formation of MGCs, initially observed in HIV-1-infected patients and in experimentally SIV-infected macaques. However, there is a paucity in the extensive characterization and formation of these MGCs in vivo in the CNS but also in other lymphoid and non-lymphoid tissues.
As macrophages are now emerging as crucial target cells involved in all stages of HIV-1 pathogenesis and in viral persistence within tissues of infected individuals, even under antiretroviral treatment, the overall aim of this ambitious proposal is **to conduct an exhaustive and systematic characterization of the mechanisms that govern, control and modulate the cell-cell fusion process for virus cell-to-cell transfer and infection of macrophages using in vivo and in vitro experimental models**.

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

Harms*, M., Smith*, N., Han, M., Groß, R., von Maltitz, P., Rodriguez-Alfonso, A., Sayettat, Lagane, B., Benichou, S., Sanchez Garcia, E., Herbeuval, J.-P. and Münch, J. (2023) Spermine and spermidine bind CXCR4 and inhibit CXCR4- but not CCR5-tropic HIV-1 infection. Science Advances, 9, eadf8251. (*equal contribution).

Mascarau, R., Woottum, M., Fromont, L., Cantaloube-Ferrieu, V., Vahlas, Z., Bertrand, F., Beunon, T., Métais, A., Poincloux, R., Lagane, B., Benichou, S., Raynaud-Messina, B. and Vérollet C. (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.

Xie, M., Leroy, H., Mascarau, R., Woottum, M., Ciccone, C., Vérollet, C., Bouchet, J., Bracq, L., and Benichou, S. (2019) Cell-to-cell fusion for HIV1 spreading and SAMHD1-independent productive infection of myeloid target cells. mBio 10(6), e02457-19.