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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
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Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : **Inserm U1016, CNRS UMR8104, Université de Paris** **Intitulé Equipe :** **Immune Cell Signalling and Viral Infection** **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 : 0140516578

Titre du projet: Characterization of cell-to-cell spreading of SARS-CoV-2 by cell-fusion

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

In addition to lung epithelial cells, lung **myeloid cells** such as alveolar macrophages are emerging as primary target cells of **SARS-CoV-2** critical for pathogenesis. Infection of alveolar macrophages by SARS-CoV-2 might be drivers of the "cytokine storm", which could result in damages in pulmonary tissues, heart, kidneys, and liver, and leads to the failure of multiple organs. Interestingly, **large multinucleated cells (or syncytia)** derived from fusion of infected epithelial cells and macrophages, have frequently been observed in the lungs of SARS-CoV-2-infected patients. Because syncytia formation was proposed to enable virus to participate in the pathogenesis of infection by increasing **viral intercellular spreading** between neighboring cells, it is therefore essential to decipher, at the cellular and molecular levels, the mechanisms that govern and modulate intercellular virus transmission between the different target cells of SARS-CoV-2. Thus, the general goal of our project is to characterize whether SARS-CoV-2 could mediate cell-cell fusion for virus cell-to-cell transfer and dissemination between its different target cells, including lung epithelial cells and myeloid cells, such macrophages, dendritic cells (DCs) and monocytes. The aims of this proposal are to investigate whether SARS-CoV-2 can trigger cell-fusion for virus transfer i) between infected and non-infected lung epithelial cells; ii) between infected and non-infected myeloid cells, including monocytes, macrophages and DCs; and finally, iii) through cell-to-cell fusion between infected epithelial cells and myeloid target cells, or conversely between infected myeloid cells and epithelial cells.
The results obtained through development of this proposal and the characterization of the experimental system should open avenues for further elucidation, both at the cellular and molecular levels, of the role played by these infected large multinucleated syncytia in viral intercellular spreading, in the destruction of alveolar architecture, in immune or inflammatory responses, as well as for virus dissemination and persistence in other tissues and organs.

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

Leroy, H., Han, M., Woottum, M., Bracq, L., Bouchet, J., Xie, M. and Benichou, S. (2020) Virus-Mediated Cell-Cell Fusion. Int. J. Mol. Sci. 21, 9644.

Xie, M., Leroy, H., Mascarau, R., Woottum, M., Dupont, M., Ciccone, C., Schmitt, A., RaynaudMessina, B., 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. mBio10(6), e02457-19.

Bracq, L., Xie, M., Benichou, S*., and Bouchet, J*. (2018) Mechanisms for cell-to-cell transmission of HIV-1. Front. Immunol., 9, 260. (*Corresponding authors)

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