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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage de M2, 2022-2023

Unité INSERM ou CNRS ou Université : INSERM U1016, CNRS UMR 8104, Université de Paris **Intitulé Equipe :** Biologie des phagocytes, Infection & Immunité **ED d'appartenance :** BioSPC **Responsable de l'Equipe :** Dr. Florence. NIEDERGANG	**Responsable du Stage :** Dr. Fatah OUAAZ **Contacts** Adresse : Institut Cochin 22, rue Méchain. 75014 Paris Email : fatah.ouaaz@inserm.fr Tel : 01 40 51 64 21

Titre du projet : Regulation and role of dendritic cell subsets in antigen transfer and activation of B lymphocytes

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

Dendritic cells (DCs) are professional antigen-presenting cells, which sample antigens (Ags) in the periphery and migrate to the lymph node (LN) where they activate T cells and potentially B cells. Previously, we have reported that human monocyte-derived DCs were able to release native Ag internalized by macropinocytosis from the late endosomes in the extracellular medium by a process that was named "regurgitation". Recently, we reported that murine DCs are important peripheral carriers of Ag to the LN B-cell zone and also potent activators of B cells both *in vivo* and *in vitro*. Importantly, we highlight that Ag released upon DC regurgitation is sufficient to efficiently induce early B-cell activation through the nuclear accumulation of the transcription factor NF-κB/cRel. However, the regulation of DC regurgitation as well as the respective role of LN-resident DC subsets in Ag transfer and B-cell activation remain poorly investigated.

On the basis of these findings, the M2 candidate will now explore: 1) the respective role of the LN-resident DC subsets (cDC1/CD8⍰$^+$, cDC2/CD11b$^+$) in Ag transfer and B-cell activation; 2) the mechanisms of the regulation/control of DC regurgitation by investigating the role of both NF-κB and Interferon pathways as well as the role of chemokines.

The candidate will use murine specific anti-HEL B cells (from MD4 transgenic mice) and DCs (Bone marrow (BM)-derived DCs; *ex vivo* purified spleen DC subsets) pulsed with Ag (HEL). He/she will explore the modalities of Ag transfer by DCs and their impact on B cell activation *in vivo* and in co-culture *in vitro* by confocal microscopy and flow cytometry. NF-κB activation will be analyzed both by western blot and confocal microscopy. All these experimental approaches are developed and available in the laboratory. We expect to provide new mechanistic insights into Ag transfer and direct B-cell activation modalities by DCs and also new approaches for NF-κB manipulation and DC targeting to elicit humoral immunity.

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

1- El-Barby H, Capitao M,....., Niedergang F and Ouaaz F (2020). Extracelluar release of antigen by dendritic cell regurgitation promotes B-cell activation through NF-κB/cRel**. J Immunol**, 205, 608-618.
2- Jubrail, J., Africano-Gomez, ..., G., Mootoosamy Cunoosamy, D., Kurian, N., and Niedergang F (2019). Arpin is critical for phagocytosis in macrophages and is targeted by human rhinovirus. **EMBO Rep**. 21, 1.
3- Niedergang F, Grinstein S. (2018). How to build a phagosome: new concepts for an old process. **Curr Opin Cell Biol**. 50:57-
4- Jubrail J, Africano-Gomez K,....., Kurian N, Niedergang F (2018). HRV16 impairs Macrophages Cytokine Response to a Secondary Bacterial Trigger. **Front Immunol**. 18; 9:2908.
5- Le Roux D, Le Bon A,....., Bismuth G, Niedergang F. (2012). Antigen stored in dendritic cells after macropinocytosis is released unprocessed from late endosomes to target B cells. **Blood**. 19, 95-105.

1 page maximum SVP !