



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

Parcours : **Biologie et Développement Cellulaires 'BDC'**

<http://www.master2bdc.fr/>

Fiche de Projet de Stage M2, Année 2020-2021

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<b>Intitulé Equipe :</b> Biologie des phagocytes, Infection & Immunité	<b>Contacts</b> Adresse : Institut Cochin 22, rue Méchain. 75014 Paris
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**Titre du projet :**

**Role of dendritic cells in antigen transport, 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. However, the mechanisms of Ag transfer and B-cell activation by DCs remain incompletely understood. Recently, we reported that murine dendritic cells 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 induce early B-cell activation through the nuclear accumulation of the transcription factor NF- $\kappa$ B/cRel.

On the basis of these findings, the M2 candidate will now explore : 1) the respective role of the LN-resident DC subsets (CD8 $\alpha^+$ , CD11b $^+$ ) in Ag transport, transfer and B-cell activation both *in vivo* and *in vitro*; 2) the intracellular mechanisms underlying Ag regurgitation by DCs through the investigation of the role of DC extracellular vesicles (EVs) and the NF- $\kappa$ B pathway in Ag release and in subsequent B-cell activation.

The candidate will use specific anti-HEL B cells (from MD4 transgenic mice) and DCs (Bone marrow-derived DCs; *ex vivo* purified spleen DC subsets) pulsed with Ag (HEL). He/she will explore the Ag trafficking by DCs and B cell activation *in vivo* and in co-culture *in vitro* by flow cytometry, immuno-histochemistry and confocal/2-photon microscopy. He/she will also measure by ELISA serum antibody production following mice immunization with HEL-loaded DCs. NF- $\kappa$ B activation will be analyzed by western blot (on nuclear extracts) and confocal microscopy and its direct role will be approached by a specific drug inhibition. All experimental approaches are available in the laboratory. We expect to provide new insights into Ag transfer by DCs and encounter by B cells *in vivo* and also new approaches for DC targeting to elicit humoral immunity.

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

- 1- El-Barby H, Captao M, Barrin S, Amziani S, Pierre-Paul P, Borreill S, Guilbert T, Donnadiou E, Niedergang F and Ouaz F (2020). Extracellular release of antigen by dendritic cell regurgitation promotes B-cell activation through NF- $\kappa$ B/cRel. *J Immunol (in press)*.
- 2- Jubrail, J., Africano-Gomez, K., Herit, F., Mularski, A., Bourdoncle, P., Oberg, L, Israelsson, E., Burgel, P-R., Mayer, G., Mootosamy Cunoosamy, D., Kurian, N., and Niedergang F (2019). Arpin is critical for phagocytosis in macrophages and is targeted by human rhinovirus. *EMBO Rep*.
- 3- Niedergang F, Grinstein S. (2018). How to build a phagosome: new concepts for an old process. *Curr Opin Cell Biol*. 50:57-63.
- 4- Jubrail J, Africano-Gomez K, Herit F, Baturcam E, Mayer G, Cunoosamy DM, 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, Dumas A, Taleb K, Sachse M, Sikora R, Julithe M, Benmerah 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 !**