



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 U1016-CNRS UMR8104-Université Paris Cité Intitulé Equipe : Biologie des phagocytes, Infection & Immunité ED d'appartenance : ED562 Responsable de l'Equipe : Me. NIEDERGANG Florence	Responsable du Stage : Mr. OUAAZ Fatah Contacts Adresse : Institut Cochin. 22, rue Méchain. 75014 Paris Email : fatah.ouaaz@inserm.fr Tel : 01 40 51 64 21
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Titre du projet :

Distribution and Role of Dendritic Cells in Antigen Presentation and B Lymphocyte Activation: Impact of Respiratory Viral Infection

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. Previously, we have reported that DCs were able to store internalized Ag by macropinocytosis that they release from late endosomes in native form in the extracellular medium, to be recognized by B lymphocytes. Later, we reported that murine DCs are important peripheral carriers of Ag to the LN B-cell zone and also potent B-cell activators both in vivo and in vitro. We highlight that Ag released by DCs is sufficient to efficiently induce early B-cell activation through the transcription factor NF- κ B/cRel. The spatial distribution of the LN-resident DCs and the respective role of the distinct DC subsets in Ag transfer and the Ag-dependent B-cell activation, however, are still unknown. Furthermore, the impact of respiratory viral infection on the re-distribution of the LN-resident DCs as well as on Ag presentation for B-cell activation still remain to be investigated.

On the basis of these findings, the candidate will now explore: 1) The spatial distribution of LN-resident DCs (cDCs and pDCs) in steady state and their respective role in Ag transfer and B-cell activation in co-culture in vitro; 2) The impact of respiratory viral infection on the re-distribution of the LN-resident DCs in vivo as well as on Ag presentation and B-cell activation in co-culture in vitro.

The candidate will use wild-type (wt) and transgenic MD4 mice, whose B cells express a BCR specific for Hen Egg Lysozyme (HEL), our Ag model. Bone marrow derived-DCs (BMDCs) and ex vivo purified spleen/LN DC subsets will be used after pulse with Ag for both in vivo and in vitro assays. Ag capture and transfer from DCs to B cells as well the subsequent B-cell activation will be assessed by Western Blot (WB), Confocal Microscopy (CM) and Flow Cytometry (FC). Viral infection of DCs will be carried out by using the respiratory Influenza A (IAV) virus both in vitro and in a mouse model of IAV infection in vivo. Activation of NF- κ B will be analyzed by WB / confocal microscopy and its direct role will be approached by a specific chemical inhibition. All experimental approaches are available in the laboratory.

We expect to provide new mechanistic insights into Ag delivery and B-cell activation by DCs as well as a new spatial re-distribution of LN-resident DCs that may impact Ag transfer and B cell activation upon respiratory viral infection with influenza virus.

We will also provide full support to the candidate wishing to apply for the doctoral school contract for a PhD position.

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

- 1- El-Barbry, H., Capitaio,, Donnadieu, E., Niedergang, F., & Ouaz, F. (2020). Extracellular Release of Antigen by Dendritic Cell Regurgitation Promotes B Cell Activation through NF- κ B/cRel. *Journal of Immunology*, 205(3), 608–618.
- 2- Martín-Faivre L, Sanchez-Guzman D, ..., Sallenave JM, Garcia-Verdugo I (2025). Pulmonary delivery of silver nanoparticles prevents influenza infection by recruiting and activating lymphoid cells. *Biomaterials*, 312:122721.
- 3- Sanchez-Guzman D, Le Guen P, Sallenave JM & Garcia-Verdugo I (2019). Silver nanoparticle-adjuvanted vaccine protects against lethal influenza infection through inducing BALT and IgA-mediated mucosal immunity. *Biomaterials*, 217:119308.
- 4- Jubrail, J., Africano-Gomez,, Cunoosamy, D. M., Kurian, N., & Niedergang, F. (2020). Arpin is critical for phagocytosis in macrophages and is targeted by human rhinovirus. *EMBO reports*, 21(1), e47963.
- 5- Le Roux, D., Le Bon, A.,, 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*, 119(1), 95–105.